

**International Symposium  
on End Results of  
Cancer Therapy**

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# **International Symposium on End Results of Cancer Therapy**

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE

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# NATIONAL CANCER INSTITUTE MONOGRAPHS

KENNETH M. ENDICOTT, *Director, National Cancer Institute*

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# **International Symposium on End Results of Cancer Therapy**

Sandefjord, Norway  
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Edited by  
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## Message of Welcome

**Karl Evang, Director General,  
The Health Services of Norway**

Mr. Chairman, Ladies and Gentlemen :

It is a pleasure to welcome you to Norway. We are honored and happy that you have chosen our country for this Symposium on the end results of cancer therapy as we now know it. If I am not mistaken, this is the first time an attempt has been made to collect data regarding survival rates of this type for nations—not for individual institutions only. Also I understand that you will even compare these national figures. This fact, among many others, reflects the unprecedented development of international cooperation in the field of medical research since World War II. As we all know, this has taken place at the *nongovernmental* as well as at the *governmental* level. The old dichotomy, the dualism between the two levels, is rapidly disappearing. In the greatest nations of the world, the development of exhaustive research programs in the field of health is now a *national responsibility* of highest priority. Casual and spotty solutions by individual scientific institutions no longer fulfill the purpose. In many countries, it is now impossible to distinguish nongovernmental and governmental scientific activities; rather, the task is regarded as a joint national enterprise. The development of epidemiology, ecology, etc., has contributed considerably to this encouraging result. However, for various reasons, international exchange of experience has not taken place to a desirable extent, and—even more—attempts at comparison between countries have been hampered. Especially in the first years of the World Health Organization (WHO), governments were rather reluctant to ask the Organization for services. Also the World Health Organization did not possess experience in methods for international health work, but this has changed completely. There are now regularly more requests for services by WHO member States than can be met within the limited financial resources of the Organization.

The data on end results of cancer therapy in the various countries obviously touch on delicate and sometimes controversial matters. Comparison of countries with respect to completeness of registration, the percentage of microscopically confirmed diagnoses, and survival rates for each country as a whole and for geographic regions within a country, is bound to bring to light differences in the organization of medical services between countries. If you go into sufficient detail you con-

tribute toward the evaluation of the quality of medical care itself. You touch on the question of competence and even on the acceptance of limitations in clinical competence on the part of both hospitals and individuals. You get material for judging the status of health education of the general population. You may even be able to demonstrate the extent to which patients fail to seek adequate service at the right time due to economic, geographic, psychological, or other deterrents. Thus, you are in the middle of the controversy concerning prepaid medical care and the ever-increasing costs of curative medicine.

We know that many of these important matters have not yet been adequately subjected to scientific research. It is high time that this is done. This is why we, the health administrators, are so interested in your work.

In this context, it is interesting to glance at the developments in medical research and health administration that have taken place in the United States during this century. In the first decades of this century, a great deal of attention in the United States was focused on the philosophy of health services called at that time "public health." Names like Haven Emerson, Winslow, Grant, and many others will remind you of that period, which represented a breakthrough in the conception of organization and functions of health services. However, contrary forces set in and the U.S. Public Health Service gradually found itself in a corner with limitations on the scope of its activities. Dr. Thomas Parran, Surgeon General at that time, and by the way, a good friend of mine, as we all know broke through this barrier with his so-called "categorical approach." What he did was to "sell" to the American Congress the idea of the necessity for research in the field of certain diseases, which for obvious reasons interested Congressmen very much. There were many of us who felt that this perhaps was a blind alley, that the U.S. Public Health Service thereby had been forced to give up its battle *in the field* and withdraw to the clear air and high ceilings of the universities and other research institutions. However, if we need any reminder of the unity of all aspects of health, this Symposium certainly is one. Through your agenda we are brought back directly into the field again, in the middle of the practical organizational economic and even medicopolitical problems of the health services of today. This time, however, we hope to have the advantage of basing our suggestions and claims for more appropriations on data.

Many of us here are in great debt to the U.S. Public Health Service and the National Institutes of Health for the support we have received directly and indirectly. As far as Norway is concerned, this is not the first time and I would like to take this opportunity to thank our American friends for their help. As a matter of fact, the joint project developed with the Norwegian Cancer Register, starting in 1959, and with considerable financial and scientific aid from the United States

has contributed toward widening the scope of work of the Register. It started in the more limited field of cancer registration but is now on its way to a full-fledged epidemiological research institution. We hope gradually to find a platform for further, more specified research and are more than happy to continue the teamwork typical of the concrete, specified, down-to-earth cooperation, which has been so well developed in the international field, and which we will also discuss informally at the Regional Meeting of the WHO in Stockholm.

Speaking of WHO, I think it is only fair to remind ourselves that one other prerequisite for a symposium of this type was the introduction in 1955 of the International Statistical Classification of Diseases, Injuries and Causes of Death through the WHO. This happened to be the second so-called "health regulation" passed by that Organization. Some of you may not be aware that its constitution in at least one important respect differs from that of all other specialized agencies.

When the constitution of WHO was drafted in Paris in the spring of 1946, the Technical Preparatory Committee, composed not of representatives of countries, but of persons in their individual capacity, agreed unanimously to try to make an end to the national anarchy which also ruled in the field of international health. Therefore the draft constitution included an article that gave the World Health Assembly the power by simple majority vote to decide on matters of international health in a way which would automatically be binding on all member States. However, when we met in New York later the same year, as government representatives, it was impossible to uphold this decision. We saved something, however, in that Article 21 states that the Health Assembly shall have authority to adopt regulations concerning a limited number of defined items important to international health. Among these items is:

(b) nomenclatures with respect to diseases, causes of death, and public health practices.

Article 22 reads as follows:

Such Regulations adopted pursuant to Article 21 shall come into force for all Members after due notice has been given of their adoption by the Health Assembly except for such Members as may notify the Director-General of rejection or reservations within the period stated in the notice.

This is one of the main reasons the health regulation on statistical classification now is used in most countries.

In spite of the encouraging development of international cooperation in the field of medical research through expert committees, seminars, symposiums, conferences, "traveling faculties," visiting scientists, fellowships, etc., we are still in the infancy of international cooperation in the field of medical research. A bold step forward is under discussion: the establishment of a World Health Research Center for the collection,



assimilation, storage, and retrieval of data and for the communication of such data to all interested parties. Certain scientific problems can only be tackled by the collection—preferably at the same time and in the same manner—of data from several countries. Also there exist certain health problems which cannot be solved at the national level due to prejudices, pressure groups, and other factors. In this connection the health aspect of human reproduction, chemical mutagenesis, and toxicities has been mentioned. Also such an international center would be a *training place* in scientific methodology for personnel both from technically well-developed and less-developed countries. I hope that you will not regard such a center, if it comes into being, as a competitor but as a body which will strengthen your own position.

Let me finish by drawing your attention to the fact that, unlike the situation on most similar occasions, the public is strongly interested in your work and the press is represented. The reason for this is, of course, that you are dealing with some fundamental problems in a way which talks directly to the public. You are not speaking of mortality, morbidity, lethality, incidence, prevalence—words which do not convey very much to the ordinary citizen. You are dealing with *prolongation of life*, with saving years; you are disproving the well-known rather pessimistic saying: "Life is the only disease for which no therapeutic remedy will ever be found."

# INTRODUCTION

## History of the Ad Hoc Group on International Cooperation in Evaluation of End Results

At the invitation of the National Cancer Institute, National Institutes of Health, USA, representatives of six national cancer registration programs met in Bethesda, Maryland, in January, 1959. The meeting was called to explore the possibility for a cooperative international effort in the evaluation of end results of cancer therapy and in the investigation of epidemiological questions. The countries represented were Denmark, England and Wales, Finland, France, Norway, and the United States.

Detailed review of the organization of each registry and of the general procedures and basic definitions revealed that there were no major differences in concepts and practices and that a productive collaborative program was feasible. Dr. John R. Heller, the director of the National Cancer Institute (NCI), indicated that NCI was prepared to give both financial and technical support to facilitate the collection and analysis of data and the organization of meetings. This policy has been endorsed and continued by the present director of NCI, Dr. Kenneth M. Endicott.

It was agreed that the Group should continue as an informal and preferably small international group of tumor registry representatives to:

1. explore areas of agreement and disagreement in the reporting of cancer, including problems of definition, nomenclature, and statistical interpretation of data;
2. develop from available data a comprehensive report on cancer end results for presentation at the Eighth International Cancer Congress in 1962; and
3. organize and analyze registry reports so as to promote the planning of special studies in end results and cancer epidemiology.

As a first step in the development of detailed plans for the collection of comparable data on end results, the late Alan McKenzie of England visited several tumor registries in the United States, and William Lourie of the United States visited each of the five European registries in the spring of 1959. These exchange visits served to identify specific areas of agreement and disagreement in definitions and procedures and helped in the development of a tentative set of rules for the compilation of data on end results.

Rules for reporting end results were agreed to at a meeting of the Group in Copenhagen, Denmark, in October, 1959. The rules included the following basic items:

1. All cases of cancer diagnosed by a physician during a specified calendar period are to be reported, whether or not they were treated.
2. Cases are to be classified as Microscopically Confirmed (biopsy or autopsy) or Not Confirmed. Cases diagnosed by exfoliative cytology only should not be classified as histologically confirmed. Cases without histological confirmation are to be tabulated separately.
3. Reporting of end results is to be restricted to new cases which received no specific treatment prior to registration. Cases first diagnosed at autopsy or registered solely on the basis of a death certificate are to be excluded.
4. A very simple staging classification is to be used—Localized (tumor confined to the organ of origin) and Not Localized.
5. The treatment recorded should be the initial, planned course and should not include treatment given on account of recurrence or further spread of the disease.
6. Every effort should be made to follow and trace each case. Cases should not be assumed to be alive solely because a death certificate has not been located.
7. Survival for a minimum of 5 years is to be calculated from date of hospital admission, from date of commencement of treatment for treated cases, or from date of diagnosis for untreated cases. Survival rates are to be corrected for normal mortality on the basis of each country's population life table. Survival rates are to be reported for cases diagnosed in a recent time period, such as 1950-54, and if possible for the years immediately subsequent to World War II, *e.g.*, 1945-49.

These rules were agreed on to achieve the greatest degree of comparability of the data from the various registries. However, it was clear from the review of specific definitions and registry procedures that there were differences which would have to be considered in the later interpretation of the data for individual sites. Some of the more important differences are discussed in the Appendix paper by William Lourie.

In planning for the Eighth International Cancer Congress, the Group decided to orient the presentation of end results data by primary site rather than by country. The sites selected for presentation were chosen to provide data for cancers with varying characteristics, *e.g.*, low incidence as well as high incidence, low survival as well as relatively high survival. The responsibility for presentation of the combined data on behalf of the Group was then distributed as follows:

Denmark	leukemia, melanoma
England	esophagus, tongue, prostate
Finland	ovary
France	breast, lung
Norway	stomach, testis
United States	cervix, corpus, large intestine, rectum

It was pointed out that the National Institutes of Health, USA, has a computer available for the calculation of survival rates. The United





Meeting of Ad Hoc Group on International Cooperation in Evaluation of End Results; January, 1959; Bethesda, Maryland, USA.  
*Left to right.*—*Front:* Einar Pedersen, Norway; W. P. D. Logan, England; Howard B. Latourette, USA; Johannes Clemmensen, Denmark; Pierre F. Denoix, France. *Rear:* George Linden, USA; Piero Mustacchi, USA; Eekki Saxén, Finland; Michael B. Shinkin, USA; Benno K. Milmore, USA; William M. Haenszel, USA; John C. Bailar, USA; Harold F. Dorn, USA; William L. Lourie, Jr., USA; Charles B. Clayman, USA; Sidney J. Cutler, USA.



States offered to do the computations for other countries, if they would convert their punched cards to conform to the computer program. Denmark, Finland, and Norway accepted the proposal.

In the spring of 1961, the Group was informed that only one session on end results of cancer treatment would be included in the program for the Eighth International Cancer Congress and that the time allotted would permit presentation of only a small part of the material being assembled. It was therefore decided to limit the presentation at the Cancer Congress to 5 sites (tongue, large intestine, breast, testis, and leukemia) and to confine the data to microscopically confirmed cases. Preliminary presentations, in advance of the Cancer Congress, were made at a meeting of the Group in London, England, in March, 1962. These presentations indicated that the rules agreed to in Copenhagen were workable and that meaningful comparisons of the results obtained in the different countries could be made.

Since only a limited consideration of end results data would be possible at the Cancer Congress in July, 1962, the American representatives suggested that a special symposium be organized for a later date. This symposium would permit a more extended presentation and interpretation of data, consideration of the implications for future work, and ample time for informal discussion by the participants. It was further suggested that the *Journal of the National Cancer Institute*, USA, be asked to publish the proceedings.

The Group accepted the proposal for a symposium on end results of cancer therapy and scheduled it for May, 1963, in Norway. (It was later postponed to September.) It was decided that to provide a complete picture of end results for each site, tabulations would be prepared for all registered cases (confirmed and not confirmed combined) as well as for those microscopically confirmed.

To provide a uniform set of tabulations of data from all six countries, the National Cancer Institute, USA, offered to process punched cards for England, France, Denmark, Finland, and Norway, provided they were converted to the "uniform code." England found it could convert punched cards on all 14 sites scheduled for analysis. France elected to convert punched cards on 4 sites (cervix, corpus, large intestine, and rectum) and to prepare tabulated data on the other sites.

It was agreed that the symposium program should be broadened to include discussion of the epidemiological and clinical implications of the end results data and that a selected group of representatives of various medical specialties would be invited to participate in the symposium.

The members of the Group met during the Cancer Congress in Moscow in July, 1962, and reaffirmed the plans for the symposium and for continued collaborative work. It was agreed that the Group should continue on an ad-hoc basis, that enlargement of the Group should be gradual, and

that participation in the program would be limited to registries that could provide the information required.

The planned symposium on end results of cancer therapy was held in Sandefjord, Norway, in September, 1963. The proceedings are incorporated in this monograph.

## **Resolutions**

The symposium participants recommended that:

1. The Ad Hoc Group should continue its efforts to develop uniform definitions and procedures to improve the comparability of data collected and published by tumor registries.
2. The participating registries, singly or in combination, should develop studies to improve the comparability of registry data and to investigate the influence of clinical, pathological, therapeutic, administrative, and epidemiological factors on end results. It is recognized that such investigations will have to be developed and carried out site by site. In decisions on the nature of problems to be investigated and on the priority for such studies, consideration should be given to the issues brought to light in the discussions at this symposium.
3. Future symposia should be organized from time to time to assess the results of special studies and to evaluate trends for selected sites with changing survival patterns.
4. Cancer registries can improve the usefulness of their data by taking advantage of information derived from studies conducted by clinicians, pathologists, and epidemiologists. Furthermore, clinicians, pathologists, and epidemiologists should be encouraged to contribute their special talents in planning and implementing studies based on tumor registry data.
5. The participating registries should investigate the interrelationship between reported incidence, survival, and mortality for individual sites to see whether they are mutually consistent.

## **Description of National Cancer Registry Programs**

To provide a background for interpreting the collected data, representatives of the six countries that contributed data were asked to describe the history and organization of their cancer registry programs. Their descriptive statements follow:



**Denmark (J. Clemmesen)**

The Danish Cancer Registry under the National Anti-Cancer League was opened in 1942. Its detailed methods were published in 1955 by Clemmesen<sup>1</sup> and will shortly be published in their revised form with full analysis of data.<sup>2</sup>

In principle this registry is run on a voluntary basis, with the assistance of public health authorities. Patients seen in hospitals are reported to the registry, both from clinical and pathological departments, and later supplemented by review of all death certificates. It is assumed in Denmark that no one is cured of cancer without hospital treatment, except a few with cutaneous cancer.

The Danish Cancer Registry has, as far as direct studies are concerned, taken an interest in etiological studies. Analyses of therapeutic results have been carried out mainly by clinicians from the respective therapeutic units, since they are in a better position to judge the uniformity of data fundamental to statistical studies. Such investigations have been supported by the information on patients' records kept in the files of the registry, which serves as a key to case records. An example of what may be achieved by this method is provided by a recent monograph by O. A. Jensen<sup>3</sup> on "Malignant Melanomas of the Uvea." The uniformity of diagnostic criteria and of therapy made it possible to treat the data from a public health as well as from a therapeutic viewpoint.

In most instances, public health interest in material covering an entire nation is concerned with the survival chances of a patient for whom the diagnosis in question has been made. The interest of the therapist will usually be restricted to survival chances with a certain treatment.

Information from a national registry will often suffice, when data contain figures for cases subject to efficient treatment and for which survival rates will mostly be known from therapeutic reports. This applies to cases of cervical cancer in Denmark, for which survival rates have been worked out for a period of 25 years through a follow-up of patients treated in 1922-29 at the Radium Hospital in Copenhagen. Results from the other therapeutic centers in Aarhus and Odense have also been reported, and clinical trials on the treatment of mammary cancer have recently been published by Kaae and Johanesen, 1963.

For the present study, the Danish Cancer Registry provided data only on specific sites for which information might be collected retrospectively, during the period at our disposal. Information on staging will be available from the files of the registry for cases seen in hospitals later than January, 1960. The sites studied were: stomach, colon, rectum, uterine cervix and corpus, leukemias, and melanomas of skin.

<sup>1</sup> CLEMMESSEN, J.: The Danish Cancer Registry. *Danish Med Bull* 2: 124-128, 1955.

<sup>2</sup> Statistical studies in the aetiology of malignant neoplasms. A report from the Danish Cancer Registry 1943-57. *Acta Path Microbiol Scand Suppl*, 1964. To be published.

<sup>3</sup> JENSEN, O.A.: Malignant melanomas of the uvea in Denmark. *Acta Ophthal Suppl* 75, 1963.

Survival time of patients was checked through the census registries. Information on stage and therapy was obtained by physicians working in the registry, who reviewed original case records provided by the various clinical services. Staging of gastrointestinal cancers was carried out on the basis of information from the operating surgical department. When the case had been regarded as radically operated it was classified as stage I (localized). For uterine cancers staging had been carried out in the clinical services for many years, according to the principles originally laid down by the League of Nations. In Denmark, therapeutic statistics on cervical carcinoma without such staging are regarded to be of limited value.

In evaluation of results, it should be noted that while the treatment of uterine carcinoma of the cervix is largely centralized in special hospitals—the so-called Radium Stations—this is not true for gastric or rectal cancer, for the calendar period under study. It may be supposed that such differences are more significant in therapeutic results than whether the patient is living in urban or rural areas.

It should also be noted that the term “known from death certificate only” stands for “not known to have been treated in a hospital,” although a small percent of cases may have been diagnosed through examination as outpatients. The percent of cases “known by death certificate only” has, during the period 1943–58, decreased from about 20 to 8 percent (Clemmesen, 1964). Seven percent of death certificates were issued by lay coroners.

### **England and Wales (L. Lipworth)**

The first step to cancer recording on a national scale was taken by the Radium Commission, which from 1930 until 1948 controlled the supply of radium to radiotherapy centers. In the years following the advent of the National Health Service in 1948, local or regional cancer registries were set up by the Regional Hospital Boards, the last in 1962. These collect information concerning cases of malignant disease in hospitals within their regions and send an abstract about each patient to the General Register Office. In the period 1945–53 there were only four local registries; in the remaining areas the General Register Office dealt directly with hospitals.

#### *Extent and Type of Coverage in 1945–53*

The limitation of cancer registration to hospitals of the National Health Service has led to two types of exclusions. The first concerns patients treated at private nursing homes, and these are considered a very small proportion of all hospitalized patients. Numerically more significant is the much larger proportion of patients not seen at hospitals before death. According to a survey in the South Western Region in 1954, these



two types of exclusions comprise 18 percent of all patients and include a high percentage of elderly patients. Unpublished information from other regions shows the percentage of nonhospitalized patients to be nearer to 10 percent.

Coverage was poor in the years 1945-49—about 20 to 30 percent of all hospitalized patients—and was heavily biased toward those treated in radiotherapy centers where registration, as just described, had been practiced since the early thirties. As a result, for several sites the percentage of registered patients with advanced disease was probably larger than it would have been had registration been complete, quite apart from the obvious underestimation of patients treated, for example, by surgery only.

The coverage also varied from region to region. In 1945 the maximum registration per thousand population in any region was 1.0. In two regions it was zero and in two others it was 0.2.

By 1953 the coverage had increased to about 50 percent of hospital cases, and the preponderance of cases notified by radiotherapy centers was less marked. The registration rates in the different regions now varied between 1.0 and 2.4 per thousand population.

### **Finland** (E. Saxén)

The Finnish Cancer Register was founded by the Cancer Society of Finland in 1952, and data on newly diagnosed cases of cancer have been collected since the beginning of 1953. The purpose of the Finnish Cancer Register is to clarify the magnitude of the cancer problem in Finland, *e.g.*, by a study of the incidence of different types of cancer in various parts of the country, and to study the possible causal relationships which may exist between environmental factors and cancer in Finland, and further to clarify and follow the possible effects of public education, preventive methods, and treatment.

The Register is headed by a Committee in which the State Medical Board, the Central Office of Statistics, the Finnish Medical Association, and the Cancer Society of Finland are represented. The costs of the Registry have been defrayed by the Finnish Cancer Register.

All hospitals, pathological laboratories, and practicing physicians in Finland have been urged to report to the Register all cases of cancer which come to their attention. (Since 1961 the reporting has been compulsory.) In addition, the register is informed of all death certificates on which cancer is mentioned. The registered cases are checked yearly against *all* death certificates issued in Finland, and for the present End Results Study a follow-up investigation was performed for all patients not known to be dead.

In reports from pathological laboratories only and notifications only from death certificates, the sender of the specimen or the signer of the death certificate is asked to supply additional information. Over 20,000 reports on about 9,000 new cases of cancer are received yearly.

If the figures presented in this monograph are used for a detailed comparison between countries, additional information should be asked from the Finnish Cancer Register.

The Finnish Republic lies between the latitudes 50°30'10" and 70°5'30". The surface area is 337,113 km<sup>2</sup>, 31,570 km<sup>2</sup> consisting of inland waters. Finland lies in the coniferous forest zone, and the predominating climatic growth is forest, which covers about 73 percent of the country. It is mainly lowland with small hills and an average altitude of 150 meters above sea level. There are no mountains such as are found in many other countries in Europe. The summer season with a mean daytime temperature of over 50° is short and lasts from 2 to 4 months. The winter season—with a mean temperature falling below the freezing point—lasts from 3 to 5 months in the South and from 5 to 6 months in the North. The population numbers 4.3 million, 30 percent of whom live in cities, but the cities are small. The average population density is low, only 33 per square mile. The race is partly East Baltic, partly Nordic. Agriculture is the principal source of livelihood.

#### **France** (R. Flamant)

The Permanent Cancer Survey was created in 1943 by Dr. Denoix. This registry covers cases seen in the 21 French Cancer Centers the institutions devoted to cancer control. These 21 Centers examine and manage more than 12,000 new cases of cancer a year.

For every new cancer case diagnosed, each Center completes a clinical and therapeutic record. The main data to be entered are sex, age, nature of first symptom, time elapsed from first symptom to examination in the center, site of origin of the tumor (classified according to a nomenclature derived from the International Classification of Diseases and Causes of Death), extent of the tumor (classified according to the T.N.M. Code), and particulars of treatment. Each year, for 10 years at most, a "follow-up record" is submitted that shows the status of the patient: alive (with or without local recurrence, with or without metastasis) or dead (with the date of death). The records are sent to the Institut National d'Hygiène, where they are verified, coded, and converted to punched cards.

This registry has two basic peculiarities: It is comparatively rich in clinical data, and that is an advantage. It is clearly biased, as the patients who come to the Cancer Centers are but a small part of patients with cancer in the general population. More precisely, they are the advanced cases which doctors are unable to manage further in private practice, and the cases amenable to radiotherapy. This is due to the technical equipment available at the Centers. On the other hand, cases amenable to surgery (particularly stomach, intestine, and rectum cancers) are comparatively rare in this group. This is an important shortcoming.

**Norway** (E. Pedersen)

The Cancer Registry of Norway has been in operation since January 1, 1952. Based on compulsory notification, the registration scheme covers the whole of Norway and aims at a complete registration of all recognized cases of cancer among the total population of the country. Reportable are all conditions classifiable under categories 140 through 205 of the International Statistical Classification of Diseases, Injuries, and Causes of Death; all kinds of neoplasms of the central nervous system; "stage 0" or "*in situ*" lesions of the uterine cervix; and papillomas of the urinary tract. Carcinoid tumors of the gastrointestinal tract are also registered, whether specified as malignant or not.

However, except for some types of tumors of the central nervous system, cases of questionable malignancy are not included in tabulations unless this is expressly stated. All such cases have been excluded from the present End Results Study.

According to rules laid down by the Ministry of Social Affairs, reports are required from: 1) all hospital departments; 2) all institutes of pathology; and 3) all institutes of radiology.

Every new cancer patient is to be reported, whether treated or not, whether occupying a hospital bed or seen only in outpatient departments. A new report is to be submitted every time a cancer patient is readmitted or re-examined for his malignant disease. Records are to be filled in and signed by a physician. Instead of submitting ordinary reports, some hospitals prefer to send in the original records of cancer patients at regular intervals, for abstracting in the Cancer Registry. Actually, the complete hospital records for approximately 30 percent of all registered cancer patients in Norway are abstracted or reviewed by a physician in the Registry.

As a consequence of the rules established for reporting cancer in Norway, most cases are reported repeatedly and from different institutions. Thus, more than 70 percent of all cases (excluding skin cancer) are initially accounted for both from a clinician and a pathologist. Such independent reporting, besides increasing the probability that all cases will sooner or later be registered, in many instances also results in more accurate and complete information than the Registry would have received if records were submitted once and from one source only.

At regular intervals, all death certificates mentioning cancer or tumor are forwarded to the Cancer Registry from the Central Bureau of Statistics, to be matched against the file of registered cases. For every case that cannot be found in the Registry, a letter is mailed to the physician who signed the death certificate asking him to assist in obtaining a complete report on the case. If necessary, the request is repeated.

The number of deaths queried per year has been gradually decreasing as registration has improved, but for the years 1953-56 approximately



25 percent of all death certificates mentioning cancer or tumor were questioned. Completed returns were received from physicians for over 90 percent of the deaths queried. Depending on the information thus obtained, it was decided for each case whether it should be accepted for registration or rejected. As a result of this procedure less than 2 percent of the cases registered as cancer in Norway are merely on the basis of the death certificate, with no additional information.

Most of the cases that are first known from death certificates have never been hospitalized for malignant disease. In most of these, the diagnosis is based on a superficial examination of patients in the terminal stage of the disease.

A more complete description of the registration system has been given elsewhere.<sup>3, 4</sup>

The Norwegian contribution to the End Results Study is confined to cases diagnosed during the years 1953-56. In connection with this study, the entire material for the 4-year period—altogether approximately 32,000 cases—was revised and recoded.<sup>5</sup> Although in many respects the code ordinarily used in Norway is much more detailed than required for the End Results Study, it failed to provide for some of the specifications requested by the Ad Hoc Group, in particular, as regards the description of stage and treatment. The main purpose of the revision was to establish conformity in the description of these two important characteristics, but it also provided an opportunity to check all other relevant information for completeness and correctness.

Some of the steps taken in preparing the Norwegian material for analysis are briefly described.

*Classification by stage of the disease.*—On the forms used for reports from clinical departments to the Cancer Registry, the physician is asked to describe the site and extent of the primary tumor. He is also asked to state whether metastases have been demonstrated, and if the answer is in the affirmative to specify their location.

In reporting the results of microscopic examination of biopsies, the pathologists are requested to state from where the specimen was obtained, of what it consisted, and, furthermore, to describe accurately the site of the primary tumor. As a rule, when the surgical specimen comprises the primary tumor, the description will include some information regarding the size of the tumor and its relationship to surrounding tissues and organs.

Based on these reports the Cancer Registry, before 1959, routinely attempted to distinguish between cases in which no metastases had been demonstrated, those with regional lymph node metastases, and those with

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<sup>3</sup> PEDERSEN, E., and MAGNUS, K.: Cancer registration in Norway: The incidence of cancer in Norway, 1953-54. The Norwegian Cancer Society, Oslo, 1959.

<sup>4</sup> ———: Cancer registration in Norway: The incidence of cancer in Norway, 1953-58. The Norwegian Cancer Society, Oslo, 1961.

<sup>5</sup> This work was carried out under contract No. SA-43-ph-3080 from the National Cancer Institute, National Institutes of Health, Public Health Service.

all other types of metastases. This stage classification refers to the time of the primary treatment or, for those who received no treatment, to the time of diagnosis.

The End Results Study required a further refinement in stage classification. Among those in whom no metastases had been demonstrated, it became necessary to distinguish between two groups, namely, those with: (a) primary tumor confined to the site (organ) of origin and (b) primary tumor infiltrating directly (per continuitatem) neighboring tissues or organs.

While the former group satisfied the Ad Hoc Group's definition of a *localized* tumor, the latter group was to be classified as "regional spread" or as "not localized," depending on the site studied.

To make this distinction, all the cases in which no metastases had been demonstrated were reviewed. For this, it was necessary to go back to the original reports from clinicians and pathologists. The review was not confined to the 14 sites studied by the Ad Hoc Group, but comprised the entire material (excluding skin cancer) of the Cancer Registry for the years 1953-56, in accordance with the conditions of the contract between the National Cancer Institute and the Cancer Registry.

*Classification by treatment.*—The classification used by the Cancer Registry is much more detailed than required for the End Results Study. A minor discrepancy in the classification of some surgical procedures necessitated a limited revision of the Norwegian material. Subsequently, the Norwegian treatment code could easily be converted mechanically to the broader categories of the Uniform Punch Card Code.

*Follow-up procedure.*—The Norwegian Radium Hospital is the only hospital in Norway that systematically follows all patients until death. About 25 percent of all cancer patients in Norway are treated at this hospital. Follow-up information on patients treated at other hospitals is received only if and when the patients are readmitted for malignant disease. This means that most patients remaining recurrence-free for a number of years after treatment are temporarily "lost sight of" by the Cancer Registry.

Information about date and cause of death of cancer patients is obtained partly from hospitals, but mostly from death certificates. As previously pointed out, the Cancer Registry receives all death certificates mentioning cancer or tumor. In addition, each year the Cancer Registry receives complete alphabetical lists of all persons having died from any cause in Norway during the specific year. Date and cause of death are given on the lists.

The special contract under which the End Results Study was carried out in Norway required that the survival status as of January 1, 1960, be ascertained for all cancer patients diagnosed during the period 1953-56. When the material was reviewed early in 1961, approximately 75 percent of the patients had died. There remained approximately 8,000 for whom

the survival status was unknown. Information about these was then requested from the respective local population registers. The query was sent out from The Central Bureau of Statistics, and not from the Cancer Registry, as it seemed desirable to conceal the nature of the study from the personnel of the local population registries. Thus, the query was indistinguishable from any other routine request for information from the central administration. The query was highly successful and less than 1 percent remained whose status was unknown.

*Processing of the material.*—The material was coded in accordance with a modified Norwegian code, the coded data were transferred to IBM cards, and then mechanically converted to the Uniform Punch Card Code. Finally, the punched cards were shipped to the National Cancer Institute, USA for further processing.

As specified in the contract, this material included all cases of cancer diagnosed in the Norwegian population during the years 1953–56 and reported to the Cancer Registry. Consequently, the material also included cases first diagnosed at autopsy, cases registered merely on the basis of death certificates, and those that had not been hospitalized for malignant disease. However, these groups were identified by the code so that for any particular analysis they could be included or excluded at will.

### **United States (S. J. Cutler)**

The Cancer End Results Evaluation Program sponsored by the National Cancer Institute of the Public Health Service is an outgrowth of the Symposium on End Results in the Treatment of Cancer at the Third National Cancer Conference, June 4 to 6, 1956. The symposium was organized to evaluate the status of survival in cancer patients at mid-century and to examine the adequacy of available data. Although it was possible to collect information on 5-year end results on 66,000 patients from 3 central registries, 11 hospitals, and 21 individual cancer specialists, a detailed analysis could not be attempted because of the limited scope of the data collected.

At an ad hoc meeting of tumor registry representatives during the Conference, it was agreed that a continuing program of cooperation and coordination among the various registries was highly desirable to develop uniform definitions, procedures, and follow-up policies, and to pool resources for research activities. The recognition, by the tumor clinic registrars, of the desirability for a coordinated data-gathering program coincided with a sizable expansion of the cancer chemotherapy research program. The rapidly growing chemotherapy research program accentuated the need for cooperative research based on long-term follow-up of cancer patients. The evaluation of chemotherapy had to be related to the end results achieved by other means of treatment. It seemed wise to build a research program for the evaluation of therapeutic end results on a co-



operative effort by well-established cancer registries. Therefore, the National Cancer Institute of the U.S. Public Health Service invited the registries that had submitted usable information to the Third National Cancer Conference to join in a cooperative program for the evaluation of end results in cancer. The National Cancer Institute offered to support the research effort by contracts providing for the submission of specified data on an annual basis, and by providing a technical and administrative staff to coordinate the activities of the individual participants. Thus, the development of the chemotherapy research program offered an opportunity to achieve at least some of the hopes and aims of the tumor clinic registrars.

A series of work-group meetings led to agreement on a uniform punched card layout and code for the submission of information on individual patients. Experience with the Uniform Code has led to revision of procedures at the individual registries to insure uniform application of agreed-upon definitions. In addition, a continuing quality control program is in operation to check on the implementation of uniform definitions and procedures.

Punched cards containing current follow-up information on each registered cancer case are submitted annually to the National Cancer Institute, until death or "permanent loss to follow-up." Punched cards on approximately 25,000 newly diagnosed cases and on 85,000 cases previously reported as living are submitted each year. Patient follow-up is 96 percent complete at 5 years and 94 percent complete at 10 years. If cancers of the skin are excluded, these percentages increase to 97 at 5 years and 95 at 10 years.

Three centralized registries and nine registries maintained in teaching hospitals are currently participating in the program. The three centralized registries are located in California, Connecticut, and Massachusetts. The institutions cooperating in the End Results Evaluation Program were selected on the basis of ability and willingness to participate. The extent to which they are representative of all hospitals treating cancer patients in the United States is not known. It is noteworthy that the hospitals participating in the Connecticut registry program account for 94 percent of the general hospital beds in the State. In addition, the registry files in Connecticut are routinely checked against the State file of death certificates. Thus, the Connecticut registry contains information on virtually every case of cancer diagnosed among residents of the State. The survival rates among cancer patients in Connecticut have been found to be almost identical to the rates obtained from the combined data from all registries participating in the program.

### **Organization of This Monograph**

The body of this Monograph consists of the papers presented at each of the sessions. In general, two types of papers are included: 1) comparison

of treatment methods and survival rates, for a specified form of cancer, in the six countries that contributed data, and 2) discussion of diagnostic problems and therapeutic techniques by a clinical specialist. The papers presented at each session are followed by a brief summary of the general discussion.

The proceedings of the sessions devoted to specific forms of cancer are preceded by a paper by William Haenszel on leads for epidemiological study derived from the data on end results.

The body of this report is followed by several appendices:

I. "Some Observations Concerning Comparability in These Data" includes a discussion of some of the problems encountered in converting data to a uniform punched card code.

II. "Computation of Survival Rates." The actuarial, or life-table, method for computing survival rates and the rationale of the relative, or corrected, survival rate are explained.

III. "Survival Tables" are a set of standardized tables for each form of cancer discussed at the Symposium. These tables contain more detailed information than that included in the individual papers. Additional data that have been tabulated, but are not included in the published tables, are described.

SIDNEY J. CUTLER  
*Editor*

## Contributions of End Results Data to Cancer Epidemiology<sup>1</sup>

WILLIAM M. HAENSZEL, *Biometry Branch,  
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THE organizers of the Ad Hoc Group were individuals whose major interests were directed to studies of cancer incidence rather than to more clinically oriented investigations of the survival experience of cancer patients. Despite this personal preference for epidemiology, the Ad Hoc Group decided that their first essay in collaboration should deal with end results of treatment, data from which are being reported at this Symposium. Several considerations influenced this choice. A controlling reason was that limited and attainable goals could be set for comparisons of survival experience. Furthermore, this was a subject for which few data were then available. While a series of reports on survival of cervical cancer patients from cooperating hospitals in several countries had been published (1) and data on other sites were available from the cancer registers in Connecticut, England and Wales, and New Zealand (2-4), these materials left many uncertainties. Comparisons of survival rates can be affected by variations in coverage and reporting of cases, by definitions of stage and treatment, and by methods used for patient follow-up. For these reasons, a cooperative study which went behind the tabulations and inquired into issues bearing on comparability of data carried great appeal.

Knowledge about international variations in cancer incidence by site was further advanced; information from vital statistics offices and cancer registers, while imperfect in many respects, had yielded a number of consistent, identifiable patterns. However, the consensus was that inquiries into reasons for the variation in cancer incidence by site among the several countries would prove too great a gamble for an initial venture. The uncertainties inherent in epidemiological studies are their attraction and despair. In embarking on them one must recognize that he sails on uncharted seas with only a rough idea as to where he will make landfall and reach port.

<sup>1</sup> This paper was originally presented at the closing session of the International Symposium on End Results of Cancer Therapy, Sandefjord, Norway, September 16-20, 1963.

<sup>2</sup> National Institutes of Health, Public Health Service, U.S. Department of Health, Education, and Welfare.



The priority accorded survival studies never implied abandonment of interest in epidemiology. Rather, it was hoped that the survival and incidence data would have complementary uses. For example, the difference in survival of cervical cancer patients in England and Connecticut had been identified by 1959. The detailed pathology review reported by Thomas *et al.* (5) was undertaken with the thought that it might elicit information leading to a reconciliation of the incidence and survival rates for the two areas, but that either positive or negative findings could set the stage for future epidemiological inquiries.

Epidemiology has been defined in many ways, but the term is used here in the conventional sense as the study of variations in incidence of disease among population groups. Variations in the clinical course of illness in patients drawn from different populations can also be studied epidemiologically, and work along these lines has in fact been proposed; one example is the investigation of survival of lung cancer patients classified by history of tobacco use (6). However, advantage will not be taken of the specialized usage of "epidemiology of survival" to evade an issue implied by the title of this paper, "Do the forces which influence the rate of tumor induction in man persist past that point to affect the subsequent course of disease in the host?" To ask this question one must accept the premise that survival experience is not determined completely by method of treatment or skill of the practitioner. One need not embrace extreme views on biological predeterminism of cancer, that the course of the disease reflects the biological characteristics of the tumor and remains unaltered by treatment (7). The presence of important treatment effects can be conceded, with the proviso that they do not overwhelm those linked with other factors.

There are several ways in which relationships between incidence and survival rates might arise, and some possibilities are catalogued below:

(a) Exogenous agent(s) increases the number of tumors appearing at a specific site in the population affected; the tumors so induced have a characteristic histology and/or site localization and survival rates different from the usual complement of tumors at this site. Incidence and survival would then be correlated, positively or negatively, depending on whether the additional tumors present more favorable or unfavorable survival experience. If the agent(s) raises incidence only, with no differential effects on histology, site localization, or survival, incidence and survival would remain uncorrelated.

(b) More widespread and/or intense exposure to an agent leads to an increment of tumors of more marginal malignant potential among less susceptible hosts. This situation would produce an inverse relationship between incidence and survival rates.

(c) Exogenous agent(s) induces tumors by an indirect route via changes in host nutrition or metabolism; changes in the host also influence tumor growth. Depending on whether tumor growth is accelerated or inhibited, incidence and survival rates would be associated negatively or positively.

For the moment let us entertain the presence of systematic relationships between incidence and survival as a working hypothesis and examine the materials prepared for the Symposium from this point of view. Admittedly, much of what follows must be regarded as speculation. The organization of table 1 was intended to highlight suggestive patterns and clues, a task different from the more detailed and cautious appraisals of the end results findings for individual sites made by the several rapporteurs. Judgments on future lines of work must often be based on imperfect knowledge, and I am resigned to acting the role assigned to me. However, I reserve the right to modify or retract at a later date statements made here.

TABLE 1.—Relative 5-year survival rates (%) in high- and low-incidence areas: esophagus, stomach, colon, rectum, lung, breast, and cervix

Site (International List Nos., 6th revision)	Five-year survival rates			
	Males		Females	
	All stages	Localized	All stages	Localized
<i>Esophagus</i> (150)				
High incidence				
Finland (1953-56)	.02(.03) (.00)	.03(.03) (.00)	.02(.03) (.01)	.03(.04) (.00)
Low incidence				
Norway (1953-56)	.01(.02) (.01)	.01(.01) (.01)	.05(.07) (.03)	.06(.08) (.04)
Connecticut (1950-54)	.03(.04) (.00)	.03(.04) (.00)	.11(.11) (.11)	.22(.11) (.43)
<i>Stomach</i> (151)				
High incidence				
Finland (1953-56)	.08(.10) (.05)	.17(.24) (.11)	.07(.08) (.06)	.15(.22) (.12)
Norway (1953-56)	.09(.13) (.08)	.24(.39) (.19)	.10(.13) (.09)	.22(.32) (.20)
Low incidence				
Connecticut (1950-54)	.13(.17) (.10)	.33(.40) (.30)	.11(.09) (.12)	.32(.24) (.35)
<i>Colon</i> (153)				
High incidence				
Connecticut (1950-54)	.36(.38) (.34)	.60(.63) (.57)	.42(.45) (.37)	.69(.75) (.60)
Denmark (1950-54)	.26(.30) (.22)	.43(.52) (.34)	.29(.34) (.22)	.49(.53) (.43)
Low incidence				
Norway (1953-56)	.25(.29) (.21)	.43(.51) (.36)	.28(.38) (.20)	.45(.63) (.31)
Finland (1953-56)	.20(.25) (.12)	.35(.42) (.23)	.21(.26) (.13)	.39(.50) (.24)
<i>Rectum</i> (154)				
High incidence				
Connecticut (1950-54)	.37(.41) (.32)	.64(.68) (.57)	.39(.40) (.36)	.64(.68) (.58)
Denmark (1950-54)	.26(.32) (.20)	.41(.51) (.32)	.32(.37) (.24)	.51(.58) (.41)
Low incidence				
Norway (1953-56)	.22(.26) (.20)	.36(.50) (.27)	.25(.31) (.19)	.37(.52) (.28)
Finland (1953-56)	.17(.15) (.19)	.26(.23) (.31)	.25(.31) (.17)	.42(.48) (.33)

TABLE 1.—Relative 5-year survival rates (%) in high- and low-incidence areas: esophagus, stomach, colon, rectum, lung, breast, and cervix—Continued

Site (International List Nos., 6th revision)	Five-year survival rates			
	Males		Females	
	All stages	Localized	All stages	Localized
<i>Lung and bronchus</i> (162)				
High incidence				
England and Wales (1952-53)	.05(.06)	.22(.26)	.05(.05)	.22(.22)
	(.04)	(.18)	(.04)	(.21)
Finland (1953-56)	.06(.08)	.09(.14)	.08(.12)	.12(.17)
	(.04)	(.09)	(.06)	(.10)
Low incidence				
Norway (1953-56)	.08(.11)	.19(.33)	.11(.27)	.22(.65)
	(.07)	(.14)	(.06)	(.04)
<i>Breast</i> (170)				
High incidence				
Connecticut (1950-54)			(.57)	(.80)
			.56(.57)	.79(.80)
			(.57)	(.79)
			(.55)	(.77)
			(.51)	(.71)
England and Wales (1952-53)			.48(.52)	.72(.75)
			(.44)	(.70)
			(.45)	(.72)
			(.61)	(.84)
Norway (1953-56)			.57(.60)	.80(.80)
			(.57)	(.82)
			(.53)	(.77)
Low incidence				
			(.58)	(.80)
Finland (1953-56)			.52(.56)	.71(.71)
			(.48)	(.67)
			(.45)	(.66)
<i>Cervix</i> (171)				
High incidence				
			(.63)	(.72)
			(.67)	(.79)
Connecticut (1950-54)			.56(.54)	.70(.65)
			(.50)	(.66)
			(.44)	(.68)
			(.64)	(.80)
			(.65)	(.80)
Denmark (1950-54)			.60(.61)	.78(.79)
			(.57)	(.76)
			(.42)	(.58)
Low incidence				
			(.57)	(.80)
			(.58)	(.81)
Norway (1953-56)			.52(.49)	.79(.78)
			(.48)	(.72)
			(.52)	(.78)
			(.46)	(.58)
			(.43)	(.58)
England (1952-53)			.42(.42)	.59(.60)
			(.43)	(.62)
			(.38)	(.57)

NOTE: Age-specific survival rates in parentheses:

Esophagus:

Under 70 years

Over 70 years

Stomach:

Under 60 years

Over 60 years

Colon and rectum:

Under 65 years

Over 65 years

Lung and bronchus:

Under 55 years

Over 55 years

Breast:

Under 45 years

45-54 years

55-64 years

65 years and over

Cervix:

Under 35 years

33-44 years

45-54 years

55-64 years

65 years and over



The data from the 6 countries (Denmark, England, Finland, France, Norway, United States) possess an important advantage for studies of incidence-survival relationships; they represent a wide range of incidence risks for several sites, greater than contrasts to be found within any one country. Inability to demonstrate in the United States urban-rural or income-class differentials in survival rates (8) may mean merely that contrasts of populations within a relatively narrow spectrum of incidence rates are not powerful enough to detect concomitant survival-rate effects. Their major disadvantage comes from the confounding introduced by variations in treatment modalities and data collection, factors which would be minimized in materials from a single country.

Of the seven sites listed in table 1, three—colon, rectum, and cervix—suggest that incidence and survival rates vary directly, three—esophagus, stomach, and lung—indicate an inverse relationship, while breast yields no consistent pattern. This first review argues against the presence of a uniform relationship between incidence and survival for all cancer sites. It is worth remarking on the differences between the upper and lower digestive tract in this respect, a feature which parallels the striking differences in epidemiological characteristics observed for these sites.

## LUNG

The lung-cancer survival rates (all ages) for Norwegian males and females exceed those for higher risk groups in England and Finland by a small, but perceptible, amount. If Kreyberg's findings (9-11) that high-risk populations present disproportionate numbers of type I tumors (epidermoid and undifferentiated carcinomas) can be shown to hold true generally, the differences in survival may also reflect factors linked with histologic type and etiology.

Several sources have indicated undifferentiated carcinomas of the oat cell variety to have less favorable prognosis than epidermoid carcinomas and adenocarcinomas (12, 13), although some uncertainty remains because of lack of uniformity in nomenclature and classification. It is conceivable that proposals for standardization of histologic typing (14) may lead to identification of subgroups of pulmonary tumors with different survival curve characteristics, control for which might go far to reconcile the survival rates between high- and low-risk countries and between males and females.

## CERVIX

Cervical cancer patients in high-incidence countries show the more favorable survival. When localized cases alone are considered, the poor results for England and Wales, having a relatively low-incidence popula-

tion, stand out. It may prove difficult to account for the low survival experience in the latter country solely in terms of delay in diagnosis and treatment, since this would imply a correspondingly poor survival for corpus cancer patients in each age group as well, which is not true. The survival pattern by age at diagnosis appears to differ between high- and low-incidence areas. In Connecticut and Denmark the adjusted 5-year survival rates decline with advancing age. The age gradient in adjusted survival is smaller in England and Norway, so that much of the over-all disparity among countries is contributed by patients under age 55.

Review of the detailed histologic characteristics of cervical cancer cases registered in Connecticut and the Southwest Region of England was remarkable for the similarities, rather than the differences, uncovered (5). In addition, none of the more refined classifications, which might discriminate between cases from the two areas, promised to have prognostic value.

We encounter here a site for which a reconciliation of survival experience may not be effected by pursuit of more information on tumor characteristics. Continuation of this line of attack seems unpromising for cervix. The age patterns for survival rates suggest as an alternative that answers to incidence-survival relationships be sought in the domain of host characteristics, including exposures to environmental agents.

## ESOPHAGUS

For males the survival contrasts for esophageal cancer are unimpressive and females provide the more suggestive result. Finnish women have high risks for this disease, and for women the range in incidence between Finland and Connecticut and Norway is substantial. In this context the higher survival rates, all stages and localized, for women under 70 years in Connecticut and Norway should be noted.

It is well known that lesions in the lowest third of the esophagus have a more favorable prognosis (15). While better data are needed to describe the anatomical distribution of esophageal lesions in each country, the fragmentary information from occasional series reported in the clinical literature would not suggest striking differences in this respect, so that control for anatomical localization seems unlikely to resolve inter-country differences in survival.

Epidermoid carcinomas comprise the bulk of esophageal cancer, and conventional histological considerations could scarcely alter the comparative situation. Whether more sophisticated readings, such as those attempted for cervix, could improve the reconciliation of female survival rates remains to be determined. The lack of success for cervical cancer and the absence of survival differentials among males argue against the expectation of fruitful results in this direction.

A role for host influences on survival rates should not be dismissed. The association of pharyngeal cancers with Plummer-Vinson disease among women (16) lends plausibility to conjectures that changes in nutritional and metabolic states might modify the clinical course for cancers of the esophagus and pharynx in this sex.

## STOMACH

The relationships of incidence and survival for gastric cancer offer some parallels to those depicted for esophagus. A small, but consistent, differential in survival in favor of low-incidence populations prevails for both sexes, for localized cases as well as for all stages, and for the numerically important group of patients over 60 years of age. The disease presents formidable diagnostic problems, and variations in quality of diagnostic evidence render international comparisons tentative and guarded.

Nearly all gastric lesions are adenocarcinomas and the degree of differentiation influences prognosis, patients with more undifferentiated tumors showing the poorest survival (17, 18). Grossly, the superficially spreading and polypoid tumors have relatively favorable survival. Efforts should be made to obtain more detailed descriptions of the gross and microscopic pathology and anatomical features of gastric tumors and the nature of their relation to survival in the several countries. Whether such factors might account for the observed differences in survival between patients from Scandinavia and Connecticut remains conjectural.

The drop in stomach cancer incidence in the United States, noted in lesser degree in certain other countries, rivals the almost universal rise in male lung cancer as the great neoplastic phenomenon of the 20th century (19, 20). No one knows why this disease has been disappearing among successively younger cohorts. An obvious question is whether cohort changes in incidence are being accompanied by changes in survival. The data cover only a short time span, but, for what they are worth, the adjusted age-specific survival rates for stomach cancer patients in Connecticut in 1945-54 were better than for cases from the same cohort diagnosed during the 1935-44 decade (21). Possible cohort effects on survival cannot be ruled out, although more prolonged observation would be required to establish this.

If continued observations on cohorts over time, with due allowance for improvements in treatment, support the geographic comparisons in describing incidence and survival rates as varying inversely, a common link with environmental factors—diet being the obvious candidate—would become a promising hypothesis. This line of reasoning would be even more attractive if the role of diet in inducing stomach cancer were thought of as mediated indirectly through nutritional and metabolic changes in the host, rather than by local action of carcinogens present in the food ingested.



## COLON AND RECTUM

Although the reported incidence of cancer of the colon and rectum is higher in Denmark than Norway, the differences in survival are not remarkable. Connecticut and Finland provide a more extreme contrast of high- and low-risk populations, and the differential in relative survival holds within each sex, at ages over and under 65, and for localized cases. The more favorable survival occurs in Connecticut, the high-incidence population, the reverse of the situation prevailing for esophageal and stomach cancer.

While most neoplasms in the colon and rectum are adenocarcinomas, the polypoid, noncircumferential tumors and those classified histologically as Type A (Dukes) are said to have very good prognosis (17). More needs to be learned about the association between anatomical location of the tumor and incidence and survival. The distribution of neoplasms in the colon and rectum has been described for occasional series, but lack of uniform classification practices, especially for lesions near the rectosigmoid junction, preclude fine comparisons. In their review of cases reported to the Connecticut and Norwegian registers, Eisenberg, Mork, and Connelly uncovered systematic differences in classification, and their corrected data indicated the Norwegian series had a higher proportion of lesions in the rectum and fewer at the rectosigmoid junction and in the sigmoid colon than the Connecticut series (22). Reclassification left virtually unchanged the figures for the upper colon. The finding which should be stressed is that the superior Connecticut survival experience prevailed at each location within the intestinal tract, leaving the summary comparison on survival of colon and rectum cancer patients unshaken. It seems reasonable to conclude that intercountry differences in survival, noted for colon and rectum, will not disappear with control for anatomical localization.

The survival experience for colon and rectum has improved markedly in the United States since World War II (23), much of which can be ascribed to advances in surgical technique and reduction of postoperative mortality. Even so, the Connecticut survival experience for 1945-49 was superior to more recent results in Finland and Norway. The Norway-Connecticut differential in survival can be reduced about one half by restricting the contrast to cases treated by "radical surgery." The proportion of cases treated with radical surgery is greater in Connecticut, and the imponderable is by what proportion could the patients so treated in Scandinavia be raised.

The current upward trend in survival for these sites constitutes a special hazard to comparative studies oriented to incidence-survival relationships, and these might well be deferred for colon and rectum until the rates stabilize in the several countries (unpublished data for 1955-59 indicate this is now occurring in the United States).



## BREAST

No obvious patterns can be discerned from the schedules of breast cancer incidence and survival, either for all stages or for localized tumors only. The two countries having populations with more unfavorable survival, England and Finland, share one common feature—a sharp decline in relative survival rates after age 55—as opposed to Connecticut and Norway which exhibit minimal differences between patients at premenopausal and postmenopausal ages. The survival for Finnish women under age 55 compares favorably with Connecticut and Norway, but the English experience at younger ages remains inferior to that recorded elsewhere. The age pattern in survival is diametrically opposed to that for cervix, where much of the poor over-all survival in England could be attributed to lower survival rates under age 55.

Observations on Japanese women, known to have very low breast cancer incidence, lend force to the notion that studies of incidence-survival patterns may prove fruitful. Data reported by the California cancer register and Wynder *et al.* (24, 25) indicate that Japanese women have very good survival. Part of the advantage arises from the higher proportion of localized tumors, but a difference in favor of Japanese women persists when the results are examined stage-by-stage.

While breast cancers can be classified according to a number of clinical and anatomical schemes, little systematic knowledge exists about their variation among countries and patient characteristics such as age. Collection of more detailed data on these points remains a task for the future.

A break in the progression of age-specific incidence for breast cancer around the time of menopause has been described by Clemmesen (26, 27). This phenomenon emerges most clearly in Denmark and Norway, where incidence rates at ages 50 to 54 are lower than at 45 to 49. In England and the United States this effect appears as a plateau in incidence rather than as an actual decrease. In the United States "Clemmesen's hook" may be more in evidence for foreign-born than for native-born women (28). While the changes in incidence in women around the age of menopause still elude precise descriptions, there can be no doubt that the slopes of the curves for age-specific breast cancer incidence differ markedly before and after menopause.

For breast cancer we are confronted by the intriguing phenomenon of diverse shifts in incidence and survival rates in women around the age of menopause in the several countries. Breast is a site known for stable patterns of incidence, mortality, and survival rates within a given population, so that any intercountry differences would seem unusual and suggestive. The effect on incidence associated with menopause has been interpreted by some as indicating a hormonal role in the initiation of breast tumors (29), and there is convincing evidence for the influence of hormonal related factors on survival of treated breast cancer patients (30).

The findings for breast cancer commented on here may prove useful for posing specific questions on incidence-survival relationships that might be investigated by resources at our disposal.

## DISCUSSION

The configuration of the data makes it hard to believe that if by some feat of magic American physicians and hospitals were transplanted to other countries, the survival rates characteristic for the United States would be reproduced. Granted, the differentials would be diminished, but would they be wiped out? The results display sufficient promise to warrant further work utilizing a joint approach to incidence and survival. No one can foretell where this will lead or guarantee that it will be productive. The undertaking remains a calculated risk.

Some of the requirements for comparative studies of incidence and survival can be specified. They will demand development of detailed protocols for individual sites, incorporating precise definitions of stage and detailed descriptions of both host and tumor characteristics. Much information could be obtained in retrospect from existing records, but other items related to characteristics of the patient could be secured only by an ongoing study. None of the registers have staff or facilities to carry on special studies simultaneously for several sites. However, work on any one site need not involve all registers, and the Ad Hoc Group might sustain two or, possibly, three investigations at any given time.

Opinions will differ on sites to be accorded priority and the desirable combination of registers for any one study, and I can only state my views. Work on cervical cancer is underway; lung and breast cancer would be my additional candidates. If the principle of selecting groups offering the greatest contrast in incidence set forth in table 1 is accepted, a choice of participating registers becomes easy.

The following considerations are advanced to support the choice of lung as a site to which the Ad Hoc Group should direct their attention:

(a) It is a site where tumor, rather than host, characteristics may provide the more important key to the synthesis of incidence and survival data from the several countries.

(b) The criteria developed by Kreyberg offer a means to standardize the classification and reporting of lung tumor types.

(c) There are indications that lung cancer survival rates vary by gross and histologic characteristics of the tumor, and the opportunity exists to determine whether the subtypes have distinctive survival curves (31) and to ascertain whether survival curve characteristics may provide information useful in classification of tumor types.

(d) It is a site for which study of "epidemiology of survival" has been seriously proposed. For example, the survival of patients classified by

history of tobacco use may clarify issues related to sex and intercountry differences in survival.

(e) Variations in incidence by smoking, residence, and occupational history appear associated in some degree with tumor type. The epidemiological study of lung cancer under way in Finland and Norway should provide additional clues on the comparative behavior of tumor types for exploitation.

(f) Finally, numerically important is a sharp rise in incidence of lung cancer in recent years, which has been the subject of intensive epidemiological study within many countries. The time seems propitious for a concerted effort to systematize international comparisons of incidence and survival and to control for tumor type in such comparisons.

Attention has been directed to breast for quite different reasons:

(a) The evidence suggests that for this site host characteristics may be a more important determinant for incidence and survival.

(b) It presents a discrete feature, intercountry differences in the pattern of incidence and survival rates before and after menopause, which can pose questions suitable for well-defined and limited investigations.

(c) Epidemiological work on breast has been at a virtual standstill in recent years and suffers from the lack of new ideas or novel findings. International comparative studies provide an opportunity to be adventurous and to strike out in new directions.

While the remarks to this point have dealt with observational data, the discussion should not close without stressing that this is a subject which could profit from close liaison among epidemiologists, clinicians, and experimentalists. The wide scope of contrasts in the data assembled by the Ad Hoc Group may suggest lines of experimental work helpful in the resolution of the epidemiological and clinical observations on incidence and survival.

Experimental carcinogenesis is an active pursuit, but it is surprising how few experiments have ever been reported on survival of test animals as measured from the date of appearance of palpable tumors. Dose-response effects in terms of tumor induction time are well established, but the early work of Shimkin, with three chemical carcinogens, showing survival—as dated from the appearance of tumors—to be independent of dose and the rate of tumor growth only slightly correlated with it, may have discouraged further efforts in this particular area (32, 33). Recent work has consistently measured survival from the date of first administration of the carcinogen and this practice can obviously throw no light on dosage-incidence-survival relationships.

The observations from the cancer registers and animal work yield contradictory findings as to the possible effects of exposure on survival time, but this anomaly might be due to the fact that the compounds studied by Shimkin appear to be proximate carcinogens acting on cells exposed to direct contact. Should the question be reopened? Can we devise experi-



ments to study the problem in other ways with agents that induce tumors not at the site of application but by more indirect pathways elsewhere in the experimental animal?

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## **Cancer of the Lung**

Lung Cancer—Evaluation of End Results. XAVIER GELLÉ and J. LEGUERINAIS,  
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Histological Classification of Lung Cancer. LEIV KREYBERG, Norway

### **GENERAL DISCUSSION**

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## **Lung Cancer—Evaluation of End Results**

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THIS report concerns one of the most dreadful sites of cancer, which selectively strikes at males: malignant tumors of trachea, bronchi, lungs, and pleura, specified as primary. The impressive increase in incidence of this disease in the last 15 years or so in all developed countries is well known. The poor prognosis for this carcinoma is confirmed by all statistical data published throughout the world. The data we offer here, derived from the registries of five countries, validate this prognosis.

This analysis deals with approximately 28,000 cases diagnosed during 1950–54. Histologically proved cancers and not confirmed tumors are dealt with separately. Data are presented for each sex and for two age groups: under 55 and 55 years and older. It was agreed to distribute the cases into two main groups; 1) localized tumors—without any mediastinal, pleural, or parietal involvement, metastases, or clinically demonstrable neoplastic adenopathy; and 2) not localized—all other cases.

Despite some differences in recording methods, the statistics of these countries allow fruitful comparisons, as the treatment of respiratory cancers is well defined and agreed upon in most countries. Five categories of therapeutic procedures were adopted for this study: 1) surgery alone; 2) radiation alone; 3) surgery plus radiation; 4) other methods (chemotherapy, hormones, etc.); 5) untreated cases.

Corrected survival rates were computed according to the life-table method. This method avoids the danger of overstating the poor prognosis of tumors among aged patients by allowance for the naturally high mortality in the older age groups.

## AGE DISTRIBUTION

The age distribution shows that the percentage of patients 55 years of age and over is, on the whole, higher in the United States than in Europe. It seems that the disease strikes sooner in Europe. The proportion of older patients (55 and over) is greater for localized than for not localized cases.

## SEX RATIO

Among the 28,000 cases studied, there were 25,000 males and 3,000 females. As shown in table 1, the ratio of male to female patients with lung cancer varied from 4.4 in Norway to 11.1 in Finland. In fact, there was considerable variation in sex ratio among subgroups within a country. For example, in Norway the sex ratio was 2 to 1 among cases without microscopic confirmation of the diagnosis and 7 to 1 among confirmed cases. In France, the sex ratio for various subgroups with respect to confirmation, stage, and age varied from 7 to 1 to 13 to 1. In the United States, one subgroup (localized cases without microscopic confirmation) yielded a ratio of 17 to 1.

TABLE 1.—Ratio of male to female patients with lung cancer, according to country

U.S. Central	U.S. Hospitals	Connecticut	Norway	England and Wales	Finland	France
5.7	11.0	6.5	4.4	7.2	11.1	9.5

## SUBSITES

It is regrettable that no study of the site of the tumor within the lung has been made. No relevant data were given in each registry's contribution. But, for further studies, this breakdown of "lung" into more detailed subsites is highly desirable, as there is a relationship (as shown in a recent study at the Institut Gustav Roussy at Villejuif, France) between the site and the survival rate: the farther from the trachea, the higher the survival rate.

## HISTOLOGY

The percentage of *histologically proved cases* differs among countries: in Norway, about 78 percent; in the United States, 75 percent; in France 57 percent; in England and Finland, less than 50 percent. On the whole, histological examinations are made less often for women than for men, except in England.

## TREATMENT

Therapeutic procedures may be summarized as follows:

## 1) Patients under 55 years of age

## (a) Localized tumors

United States and Norway—more than half by surgery; the remaining cases distributed among no treatment, X rays, and X rays plus surgery.

England—two thirds by surgery; the remaining third divided between X rays and X rays plus surgery (confirmed cases).

Finland—X rays for 42 percent of the patients.

## (b) Not localized tumors

United States—one fourth treated by surgery, one fourth to one third not treated, the remainder treated by X ray.

Norway, England, and Finland—40 to 50 percent treated by X ray and over one third untreated. Surgery was resorted to in about 15 percent of the cases (confirmed)

## 2) Patients 55 and older

(a) Histologically *confirmed* cases

Surgery rather rare and treatment chiefly directed toward X rays or abstention; especially true in not localized tumors.

(b) *Unconfirmed* cases

From 20 percent of the patients (in the United States) to 50 percent (in England) directed toward X-ray therapy, while abstention found for two thirds to three fourths of the cases.

## RESULTS

End results vary considerably according to several factors, and their analysis reveals the following:

(a) *Period*

Patients treated in the most recent period (after 1950) have results somewhat better, and this holds for all registries which have provided data for two periods.

(b) *Age*

Younger patients (under 55) have better survival rates than older patients, and this is true for localized as well as for not localized cases.

(c) *Histological confirmation*

Generally, unconfirmed cases show a survival rate significantly inferior to the histologically proved. We evidently are dealing with patients who "from the start" are different, and the fact that one does not ascertain the histological type of their tumor expresses in some way a bad prognosis. We cannot speak of the

histological type, though it certainly affects the prognosis, since it was not given in the tabulated data.

(d) *The spread of the tumor, or stage* (see table 2)

Five-year survival rates usually are 5 to 6 times higher for localized than for not localized cases. They may even be 8 times higher.

(e) *Type of treatment* (see table 2)

The results are especially poor after X-ray therapy. Surgery alone is able to give interesting survival rates, which may reach up to 44 percent as in Norway for localized cases; in France and Connecticut the proportions are roughly comparable. Even with cases not localized, surgery gives valuable survival rates, which reach up to 18 percent in England. The Norwegian and English registries show the best results in cases where patients underwent surgery: 30 percent 5-year survivals. This is the "cure" rate generally reported by the majority of the studies based on homogeneous statistics. The X ray plus surgery combination, rarely used in the United States and Norway, gives rather interesting results in France and Finland: 17 to 18 percent survivals in localized forms, 11 to 13 percent on the total of cases. Finally let us stress the huge, and perhaps regrettable, proportion of *untreated patients*. Their survival probability is very poor, especially for not localized forms, for which the 5-year survival rate does not exceed 1 percent.

TABLE 2.—Five-year survival rates according to the stage of the lesion—selected from different countries

Males, all ages—histologically confirmed				
Surgery	Localized	0.30	0.26	0.44
	Not localized	0.12	0.10	0.12
X rays	Localized	0.02	0.03	0.06
	Not localized	0.00	0.01	0.03
Treated plus untreated	Localized	0.16	0.13	0.25
	Not localized	0.03	0.03	0.03

(f) *Sex* (see table 3)

Apparently, the results of treatment in the pulmonary site, as well as in other sites, are significantly better for females, except in England, where they are identical with those of males.

General results are as follows (see table 3): For the total of male cases, all ages, all stages, treated plus untreated, the 5-year survival rate varies from 4 percent, Connecticut, to 8 percent, Norway. The weighted mean is somewhat over 5 percent. For females, this average figure attains 8 percent.



TABLE 3.—Five-year survival rates for all diagnosed cases, by sex

Sex	U.S. Central	U.S. Hospitals	Connecti- cut	Norway	England and Wales	Finland	France
Males	0. 05	0. 06	0. 04	0. 08	0. 05	0. 06	0. 05
Females	0. 10	0. 11	0. 11	0. 11	0. 05	0. 08	0. 10

In conclusion, the extremely poor prognosis of lung cancer is reiterated. This prognosis is not mitigated even by the most modern therapeutical procedures. Thus, to say nothing of the early detection problem, since treatment gives little hope, it would be the best strategy to concentrate our efforts on prevention. A fight against air pollution, and perhaps still more against the abuse of cigarette smoking, should provide us with the best weapons against this plague of the 20th century.



## Histological Classification of Lung Cancer

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IN the study of the prognostic and therapeutic aspects of malignant tumors, the role of the pathologist is universally recognized:

1) The *diagnosis* generally is not accepted without a microscopic confirmation.

2) The correctness and value of *staging* depend greatly on the skill and care of the pathologist.

3) The *grading* of a tumor is a more intricate question, as this process involves evaluation of several characteristics. However, terms and descriptions useful in one tumor lose their significance in connection with another:

(a) A large number of mitoses in a tumor traditionally has been accepted as an expression of rapid growth. Systematic studies in our institute have, however, shown that care must be exercised in the interpretation of such findings. The number of mitoses in a tissue observed at a given moment cannot, without reservation, be used as a measure of the rate of cell renewal. A high mitotic count actually can be the result of a slow mitotic process, as well as of a high rate of cell renewal. If the process of mitosis is totally blocked, as with the Colcemid technique, we actually use the high mitotic count as an expression of the blocking itself. When the real rate of cell renewal in a tumor is studied, one has to know both the mitotic count and the mitotic duration. Recently, in a study of a mouse carcinoma induced by methylcholanthrene, this particular tumor had a cell renewal rate significantly slower than the normal epidermis, in spite of the relatively high number of mitoses.

This explains some clinical observations in which a high number of mitoses have been seen (*i.e.*, in basocellular carcinomas) despite evident slow growth; vice versa, rapid growth has been found, despite very few mitoses, at time of observation.

(b) *Great polymorphism* is seen in many highly malignant tumors as well as in very innocent neoplasms, *e.g.*, in certain Schwannomas or benign nevi.

Grading, finally, may also lead into the borderline of another mode of classification, namely, typing. The term grading should be used only to distinguish individual differences within a fairly fixed histological entity.

4) *Histological typing* aims at a classification of such tumor entities, where certain common histological characteristics are found connected with certain biological properties.

With the usual general qualification regarding technical limitations and transitional or borderline conditions, the tumors of the skin, for very useful practical purposes, can be separated as basocellular carcinomas, epidermoid carcinomas, and malignant nevus cell tumors (pigmented or unpigmented).

No fruitful study of pathogenesis, etiology, treatment, prognosis, and therapeutic end result could be undertaken if these tumors were lumped together under the term "skin cancer." In other organs similar entities can be separated, *e.g.*, in the uterus, ovaries, testis, and other organs.

For some 40 years the lump term "lung cancer" has generally dominated statistics and references, even though pathologists unconsciously have been playing with more specific terms since the first attempt at a rational classification by Marchesani in 1924. In the last decade, the great interest in the "lung cancer" problem, caused by the rapidly growing number of victims, has brought the need for a more rational classification into focus, especially after the more precise statements and findings by Kreyberg (1), Wynder and Graham (2), and Kreyberg (3).

The World Health Organization (WHO) in 1956 adopted the general problem of histological definition of cancer types and the facilitation of a uniform nomenclature. This was considered by the Study Group of Histological Cancer Types, meeting in Oslo in 1957. The further development has been the establishment of several International Reference Centres with the purpose mentioned. The first was the Lung Cancer Centre in Oslo, created by WHO, after recommendation by the Expert Committee on Cancer, 1958. This Expert Committee also laid down the Tentative Classification of lung cancer, which now with slight modifications has been tested and the results presented in a Monograph by Leiv Kreyberg (4).

The main findings are summarized as follows:

Objective criteria permit an unequivocal specific typing in more than 90 percent of ordinary routine lung cancer material.

These characteristics permit a grouping of the types in such a way as to provide a useful means for the study of etiological, epidemiological, and endemiological aspects of the lung cancer problem.

Our conclusions are valid on the statistical plane, but no such claim is advanced that every individual tumor today can be correctly typed.



The typing mentioned has been used to a limited degree also in connection with evaluation of therapeutic results as presented by Cappelen, Efskind, and Poppe (5). They examined 479 cases, 86 percent of which were typed according to the WHO tentative classification. The conclusions were: The histological type of the tumor has a decisive influence on the prognosis. The different types of lung tumors show a marked variation in their tendency to spread.

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- (3) KREYBERG, L.: Brit J Cancer 6: 112, 1952.
- (4) ———: Acta Path Microbiol Scand (Suppl) 157: 1962.
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## Summary of General Discussion

Attention was drawn to the interrelationship between the results observed in patients treated by a specific treatment method and the frequency with which that method was used. Thus, the survival rates for lung cancer patients treated by surgery were higher in countries in which a small percentage of patients were treated surgically. It is therefore important to interpret the results for a specific treatment method in the light of the results for all diagnosed cases.

Histological typing of tumors of the lung is of great significance. In the past, pathological classification has been more related to morphology than to etiology and prognosis. For the latter purposes, the classification of lung tumors introduced by Kreyberg seems to be useful. It was asked whether the Kreyberg typing would depend on the number of slides and the type of specimen examined. It was stated that the diagnosis would rarely vary from one slide to the other from the same specimen, or from one specimen to the other from the same patient. In some autopsy cases problems might arise because of autolytic changes and biological destruction of the cells.

Results from a recent study on a blind comparative examination of lung tumors were reported. The study had been undertaken by Kreyberg and American pathologists. The results showed a high degree of agreement between the pathologists and consistency in the classification of specimens obtained in various ways from the same patient (biopsy, operation, and autopsy). The possible use of histochemical methods was also briefly discussed.

The location of the tumor is associated with survival. For the same histological type, the more distal tumors have a better prognosis. Survival rates differ by sex. Higher survival rates in females were found in all the series presented except that from England and Wales. It was suggested that the smoking habits of English women may provide an explanation and that this hypothesis should be investigated.

The distribution of histological types in the two sexes was different. However, this could not account for the higher survival rates in females. A study in the United States had shown that, when the data were subdivided by stage and histological type, survival rates for females were consistently higher.

It was suggested that the relationship of smoking history to the survival of patients with lung cancer should be investigated. The demonstration of an association would add to the evidence on smoking as an etiological factor. Material from l'Institut National d'Hygiene in Paris had not

disclosed any difference in the prognosis of smokers and nonsmokers among lung cancer patients. The group felt that corresponding studies in other countries would be valuable.

Low survival rates in countries with high lung cancer incidence may be due to the development of a second independent tumor. Thus, observed low survival may not reflect the efficacy of treatment of the initial tumor.





## Cancer of the Uterus

Survival of Patients With Cancer of the Uterine Cervix and Corpus.  
JOHN C. BAILAR III, USA

Comparison of the Pathology of Cervical Cancer in Connecticut and the Southwest Region of England. LOUIS B. THOMAS, USA, JOHN C. BAILAR III, USA, and ANDREW D. THOMSON, England

Criteria for Evaluating Treatment. KARL KARLSTEDT, Sweden

Clinical Trials on the Treatment of Cervical Carcinoma, Stage I. ODDMUND KOLLER, Norway

Results of Treatment of Adenocarcinoma of the Uterine Body. ODDMUND KOLLER, Norway

### GENERAL DISCUSSION

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Presented at the International Symposium on End Results of Cancer Therapy,  
Sandefjord, Norway, September 16-20, 1963.



## **Survival of Patients With Cancer of the Uterine Cervix and Corpus**

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### INTRODUCTION

THE End Results Program has provided us with survival information on large numbers of cancer patients, including more than 40,000 with cancer of the uterine cervix and more than 13,000 with cancer of the uterine corpus. What can be learned from this vast pool of information? Before answering this question, it is necessary to ask other questions regarding the operation of the data collection system and the importance of various sources of error and bias.

#### Quality of Data

Is the End Results series representative of any defined group of cancer patients? Those reported from France and the United States, excluding Connecticut, are drawn from selected and perhaps unrepresentative patient populations, but data from the other sources include a high proportion of all known cancer patients in the corresponding areas. Table 1 shows the number of uterine cancer patients reported in the End Results series and the number of deaths certified to uterine cancer in official mortality tabulations for corresponding years in these five areas. Cervix and corpus are pooled because of the large number of deaths reported as "cancer of the uterus" without assignment to cervix or corpus. For any area with complete reporting of uterine cancer, the number of deaths from cancer of the cervix or corpus should be roughly half the number of patients, since about half of such patients succumb to their disease. The data in table 1 suggest that case reporting is fairly complete in Connecticut, Denmark, Finland, and Norway and about 50 percent complete in England

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TABLE 1.—Number of reported cases and number of deaths, cancer of the uterine cervix and corpus, in various areas

Geographic area	Time period	Reported cases, End Results tabulations*	Reported deaths, official mortality tabulations†
Connecticut	1950-54	2191	902
Denmark	1950-54	4886	2442‡
England and Wales	1952-53	7515	7901
Finland	1953-56	2209	1141
Norway	1953-56	1948	973

\*All cases reported by hospitals, uterine cervix and corpus combined.

†Sources: (1) and (2). ISC rubric 173 (primarily malignant chorionic tumors) included for Connecticut; excluded for other areas.

‡Mortality data for 1950 not available; 1951-54 total inflated by 25 percent to estimate 1950-54 total.

and Wales. More detailed English data, not given here, show that the deficit in reporting is probably greater for corpus tumors than for cervical tumors, but that for both sites the patients included are fairly representative of the total.

For Norway and Denmark, a check on the over-all survival figures for cervical cancer is possible. The well-known and respected Stockholm reports (3) have served for over 25 years as a model for reporting survival rates and as a standard for judging results of treatment. Table 2 summarizes recent survival information for one Norwegian and three Danish hospitals, as given in the twelfth Stockholm report. The single Norwegian hospital treats nearly all cervical carcinomas in Norway; the three Danish hospitals are responsible for all the radiation therapy given in Denmark but report few of the patients treated surgically. Thus, there should be close correspondence with the End Results tabulations for all cases in Norway and for radiologically treated patients in Denmark. Despite differences in time periods included and in small variations in the definition and calculation of survival rates, the rates reported for Denmark and Norway are indeed similar in the two sources.

Thus, comparison of the End Results tabulations with official mortality tabulations and with the twelfth Stockholm report suggests that the data reported for Connecticut, Denmark, Finland, and Norway are complete and representative of the corresponding populations, and that the English data include approximately half of all cases occurring in England and Wales.

A second question is whether the information on age of patients, stage of cancer, treatment method, and other items is accurate. A detailed review of hospital records and other documents in Connecticut (5) showed that there was no significant reporting bias in the age of patients or in the year of diagnosis, and it seems unlikely that there have been serious errors in these items in the other geographic areas. Information on type of primary treatment and on histologic type is also probably accurate, but is somewhat incomplete in the End Results tabulations.



TABLE 2.—Crude 5-year survival rates\* for cancer of the uterine cervix reported in the twelfth Stockholm report † and in the End Results tabulations, for Norway and Denmark

Source	Year of diagnosis or treatment	All stages				Localized tumors ‡			
		All cases		Radiotherapy only		All cases		Radiotherapy only	
		Number of patients	5-year survival (%)	Number of patients	5-year survival (%)	Number of patients	5-year survival (%)	Number of patients	5-year survival (%)
Norway, Stockholm report	1950-54	1225	50.9	1082	45.6	310	77.1	195	72.8
	1953-56	1273	49.0	989	44.6	337	76.4	167	67.0
Denmark, Stockholm report	1950-54	2789	55.8	2777	53.3	786	72.5	775	72.4
	1950-54	3568	56.4	2790	57.5	1126	75.0	734	74.7

\*Calculated as follows: End Results tabulations: Percent of patients alive at 5 years, with or without cancer, calculated by the actuarial method (4). Stockholm report, "All stages, all cases" category: Percent of patients known to be alive at 5 years, with or without cancer, plus those lost. There were 14 patients lost in Denmark, none in Norway. Stockholm report, "All stages, radiotherapy only" category plus both categories with localized tumors: Percent of patients known to be alive at 5 years with no evidence of cervical cancer.

†Source: (3). Norway, hospital 61 only; Denmark, pooled data for hospitals 24-26.

‡Corresponds to stage I in these hospitals.

Microscopic verification of cancer is missing for 9 percent of patients, and 8 percent of patients fell in the category of "no known treatment." Since 5-year survival in the latter group was about 15 percent, many of the patients must have had some sort of definitive therapy.

Another difficulty is in the diagnosis of malignancy of various neoplasms in both cervix and corpus. Carcinoma *in situ* of the cervix and certain adenomatous polyps of the endometrium have many of the microscopic features of malignant tumors but do not metastasize and kill. Such tumors were to be excluded from the End Results tabulations, but it is possible that in some geographic areas significant numbers were reported as invasive cancers. If this occurred, it would artificially raise the reported survival rates in those areas.

In several areas, and in Connecticut particularly, a few tumors were reported only as cancer of the uterus. These cases are largely due to laziness or carelessness in reporting. The true site of origin of uterine tumors is known or can be determined in at least 95 percent of cases, but many physicians habitually say "cancer of the uterus" when they mean "cancer of the uterine corpus." In the End Results tables, all tumors of unspecified site have been combined with corpus. Although a few tumors arising in the cervix have probably been misclassified by this procedure, the resulting errors are not as great as if the unspecified tumors were omitted when survival rates were calculated.

The only other item for which there is reason to suspect serious reporting errors is tumor stage. Determination of the extent of malignant neoplasms is notoriously difficult even for such readily accessible sites as the uterine cervix and corpus. For cervix, the proportion reported as localized varies from 26 percent in Norway to 71 percent in Finland; for corpus the corresponding range is 64 percent (England and Wales) to 80 percent (Finland). Do these differences reflect real variation from one area to another in the stage of cancer at diagnosis? The answer to this question is not known, so there will necessarily be some uncertainty in the interpretation of reported survival rates, even when attention is confined to the rates for all stages combined.

Before discussing the survival rates, it is well to note some of the other limitations of the data: They refer only to patients admitted to hospitals; they come from a few areas where standards of diagnosis and treatment may be presumed to be above average and hence not representative of other parts of the world; there is no attempt to provide detailed treatment information; follow-up is less complete in some areas than in others; and there is no information on cause of death or on recurrences among patients still alive. Attempts to collect information on patients not reported by hospitals, such as those made by the Norwegian registry, have the paradoxical effect of lowering reported survival rates in comparison with registries with less complete inclusion of cases.

## General Survival Patterns

In all the following discussion, survival data will be given in the form of relative survival rates (4) unless otherwise specified. In addition, most of the discussion will be based on patients from the five areas thought to have complete or at least fairly representative reporting; that is, from Connecticut, Denmark, England and Wales, Finland, and Norway.

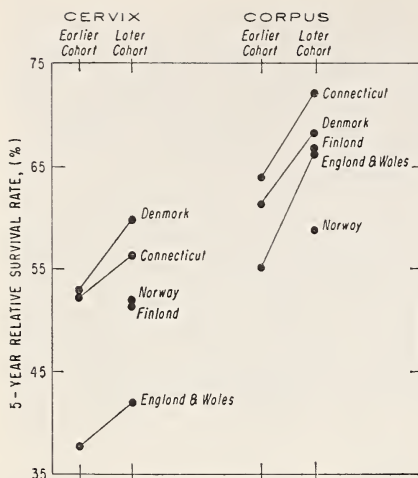
Cervical cancer differs from cancer of the uterine corpus in usual cell type, average age of patients, extent and method of spread of the tumor, and in many other features. Despite these differences, there are some similarities which make it useful to discuss cervical and corpus cancer together (table 3). Comparison of the survival of cervical cancer patients with that of corpus cancer patients, made in the light of these similarities and differences, may provide some clues for improving the survival of both groups.

TABLE 3.—Most important similarities and differences between cervical cancer and corpus cancer

	Cervical cancer	Corpus cancer
Similarities		
Site	Uterus (cervix)	Uterus (corpus)
Incidence rates	Moderately high to high	Moderately high
Patient survival	Relatively good	Relatively good
Most common symptoms	Bleeding, leukorrhea	Bleeding, leukorrhea
Accessibility to diagnosis and treatment	Easy	Easy
Treatment	Radiation usually preferred; surgery common	Surgery usually preferred; radiation common
Differences		
Usual histologic type	Squamous cell carcinoma	Adenocarcinoma
Patient age	Over 30% below age 45	Under 10% below age 45
Etiologic factors	Mostly environmental	Unknown; probably mostly internal (genetic and hormonal)
Clinical stage (pretreatment)	25-50% confined to uterus	85-90% confined to uterus

Text-figure 1 shows over-all relative survival rates for uterine cancer in these five areas. The rates are given for both cervix and corpus, and for patients diagnosed in two different time periods (cohorts) where these are available. The most obvious features here are not surprising: Survival for cervical cancer patients has been fairly good relative to that for other forms of cancer, survival of corpus cancer patients was even better, and there were significant improvements in survival for both forms of cancer from the first to the second cohort. Other points to note are that Denmark and Connecticut had the highest survival rates for both cervix and corpus, and that for each site there was one area with survival rates significantly lower than those reported elsewhere. Study of the unusually low survival of cervical cancer patients in England and Wales, where corpus cancer patients' prognoses are about average, might provide some





TEXT-FIGURE 1.—Five-year relative survival rates in various areas and time periods (1), cancer of the uterine cervix and corpus (2).

(1) Earlier cohort: Connecticut and Denmark, 1945-49; England and Wales, 1948-49. Later cohort: Connecticut and Denmark, 1950-54; England and Wales, 1952-53; Finland and Norway, 1953-56.

(2) All cases reported by hospitals, confirmed plus not confirmed, treated plus untreated.

leads for improving the survival of patients there and elsewhere. Similarly, it would be very helpful to know why corpus cancer survival rates are so low in Norway, where rates for cervical cancer are about average.

To put this problem in perspective, table 4 compares relative survival rates reported for Connecticut, Denmark, England and Wales, Finland, and Norway for several other sites of cancer. This table includes all sites reported by each of the five areas. It is clear that neither Norway nor England and Wales has consistently or unusually low survival rates for patients with cancer of sites other than cervix and corpus.

## CORPUS CANCER

### Geographic Variation in Survival of Corpus Cancer Patients

Text-figure 2 shows relative survival rates of corpus cancer patients for the first 10 years after diagnosis. The relative survival rates at 5 years ranged from 58 to 72 percent, corresponding to unadjusted 5-year survival rates of 52 and 64 percent. These survival rates are in the range of those commonly reported in the medical literature.

Text-figure 3 shows how survival and mortality varied with time after the diagnosis of cancer. As one might expect, the heaviest mortality was in the first year, and survival rates generally improved in each of the next few years. However, after 4 years there was little further improvement. The interval survival rates show that survival stayed slightly below that of the general population for 10 years or more after diagnosis, at least in the two areas for which long-term follow-up was reported. This late excess mortality of corpus cancer patients has been previously noted in Connecticut and elsewhere. An earlier study for the Connecticut data



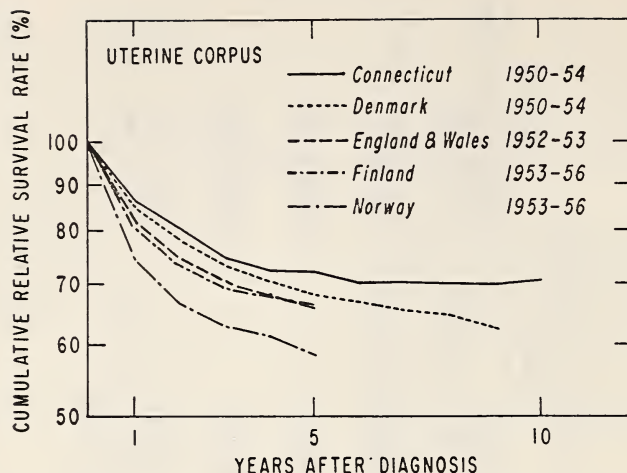
TABLE 4.—Comparison of 5-year relative survival rates\* for specific forms of cancer in various areas†

Site of cancer	Highest‡	Second	Third	Fourth	Lowest‡
Uterine cervix	Denmark (60)	Connecticut	Norway	Finland	England and Wales (42)
Uterine corpus	Connecticut (72)	Denmark	Finland	England and Wales	Norway (59)
Stomach	Connecticut (13)	Denmark	Norway	Finland	England and Wales (7)
Male	Denmark (12)	Connecticut	Norway	England and Wales	Finland (7)
Female					
Large intestine	Connecticut (36)	England and Wales	Denmark	Norway	Finland (20)
Male	Connecticut (42)	England and Wales	Denmark	Norway	Finland (21)
Female					
Rectum	Connecticut (37)	England and Wales	Denmark	Norway	Finland (17)
Male	Connecticut (39)	England and Wales	Denmark	Finland	Norway (25)
Female					
Melanoma	Connecticut (49)	Norway	England and Wales	Denmark	Finland (34)
Male	Connecticut (61)	Denmark	Norway	England and Wales	Finland (48)
Female					

\*Data from more recent cohort: Connecticut 1950-54; Denmark 1950-54; England and Wales 1952-53; Finland 1953-56; Norway 1953-56.

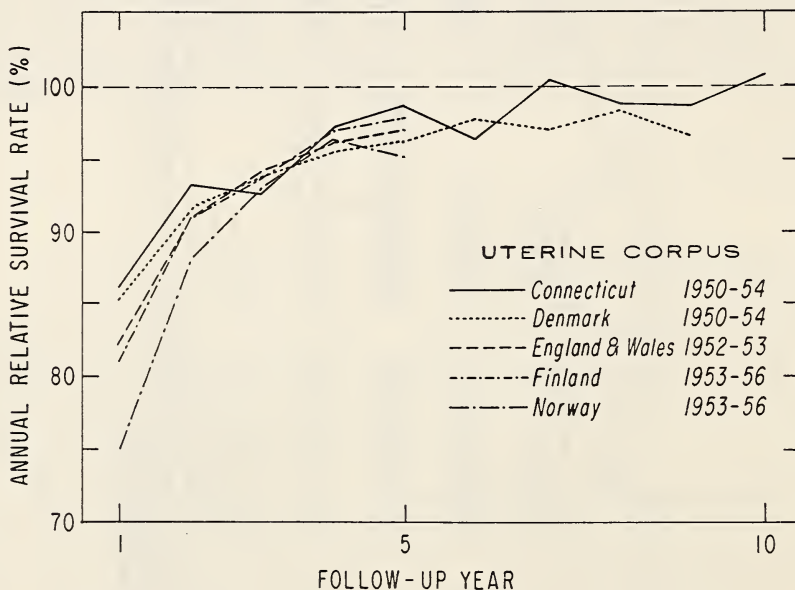
†All cases reported by hospitals, confirmed plus not confirmed, treated plus untreated.

‡Figures in parentheses indicate percent.



TEXT-FIGURE 2.—Relative survival rates 0-10 years after diagnosis, in various areas, cancer of the uterine corpus (1).

(1) All cases reported by hospitals, confirmed plus not confirmed, treated plus untreated.

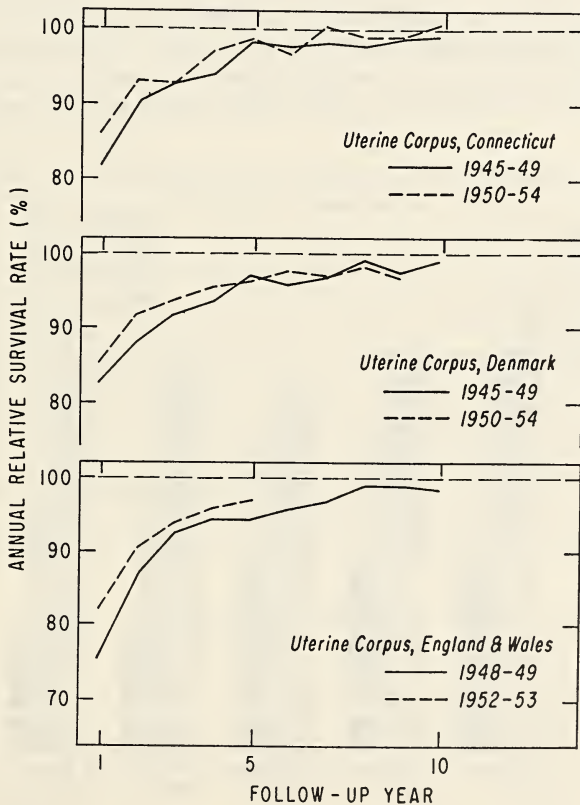


TEXT-FIGURE 3.—Relative survival rates for each follow-up year 0-10 years after diagnosis, in various areas, cancer of the uterine corpus (1).

(1) All cases reported by hospitals, confirmed plus not confirmed, treated plus untreated.

for 1935–51 (6) showed that the excess persisted for at least 20 years after the original diagnosis and treatment of cancer, that it was largely or entirely due to late recurrences and metastases of corpus cancer, and that it was related, at least in part, to the method of treatment used.

For three areas—Denmark, Connecticut, and England and Wales—we have survival rates in two different time periods. Text-figure 4 shows that there was substantial progress in reducing mortality from corpus cancer in each of these areas. Mortality was reduced in each of the first 4 or 5 years and, in Connecticut at least, the improvement may have extended for at least 10 years after the diagnosis of cancer. This may indicate a decrease in mortality from late recurrences and metastases in Connecticut, as well as the more generally known reduction of mortality in the first few years after diagnosis. Text-figure 4 does not suggest a similar



TEXT-FIGURE 4.—Relative survival rates for each follow-up year 0–10 years after diagnosis, in various areas and time periods, cancer of the uterine corpus (1).

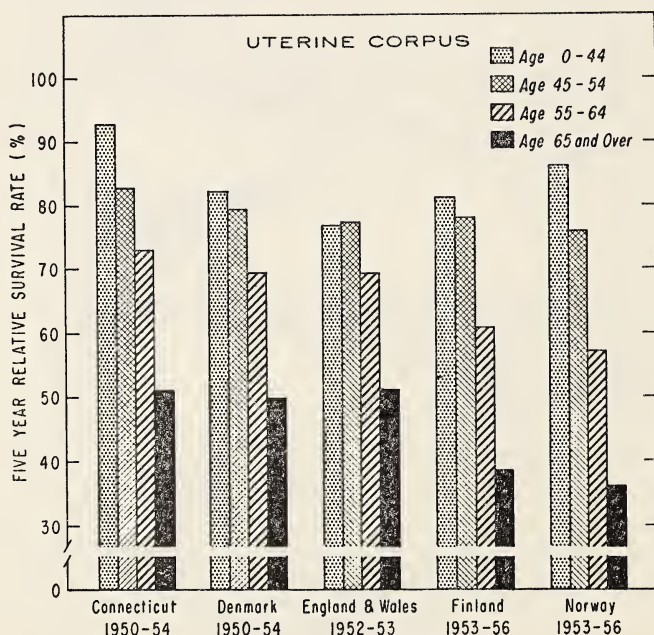
(1) All cases reported by hospitals, confirmed plus not confirmed, treated plus untreated.

decrease in late mortality in Denmark, where relative survival rates more than 4 years after diagnosis seem to have been about constant from the first cohort to the second.

### Survival and Age of Corpus Cancer Patients

Text-figure 5 shows how the 5-year survival of corpus cancer patients depended on their age at the time of the diagnosis of cancer. These are relative survival rates, so they are already adjusted for the higher "natural" mortality of older persons. Women in the youngest age group generally had the best survival rates, with progressively greater mortality at older ages. In Norway and in Finland, the 5-year relative survival rate of patients over 65 years of age was less than half that of patients under 45 years; the age differential in the other areas was smaller but still very substantial. Survival rates for separate stage groups (localized and not localized) show a similar correlation between age and survival.

On comparing age-specific survival rates for the five geographic areas, one notes that Connecticut has the highest survival rate in each of the four age groups, and Norway the lowest survival rate in the three older



TEXT-FIGURE 5.—Five-year relative survival rates by age at diagnosis of cancer, in various areas, cancer of the uterine corpus (1).

(1) All cases reported by hospitals, confirmed plus not confirmed, treated plus untreated.



age groups. However, for patients under 45 years of age Norway is second only to Connecticut. This deviation from the generally low survival of Norwegian patients with corpus cancer may be the result of small sample size since there were only 35 Norwegian patients aged 0-44 years.

One other point should be noted. Age group by age group, Norway and Finland have similar survival rates. This suggests that the difference in over-all 5-year relative survival rates (59% in Norway; 67% in Finland) may be the result of a differing age distribution of patients; this is in fact true. The Finnish population has a much higher proportion of young persons than the Norwegian population so that, despite a similarity in age-specific incidence rates in the two countries, corpus cancer patients in Finland are in general considerably younger than those in Norway. The median ages in the End Results series were 55.4 years and 59.2 years, respectively. The effect of this difference in age can be removed by the use of age-adjusted survival rates, using either the crude or the relative survival rates for each age group. Such age-adjusted survival rates are given in table 5. After the effect of differences in the age distribution of corpus cancer patients was removed, survival in Finland was similar to that in Norway, and both were significantly lower than survival in the remaining three groups.

This illustrates the necessity for relating observations on survival rates to the age distribution and other demographic features of the population from which the cases were drawn. Here, large differences in the age structure of the populations in two areas have produced a large difference in over-all relative survival rates, even though age-specific survival rates in the two areas are similar. This correlation between survival and age is *independent* of "expected" mortality from causes other than cancer, and was not removed by the use of relative survival rates.

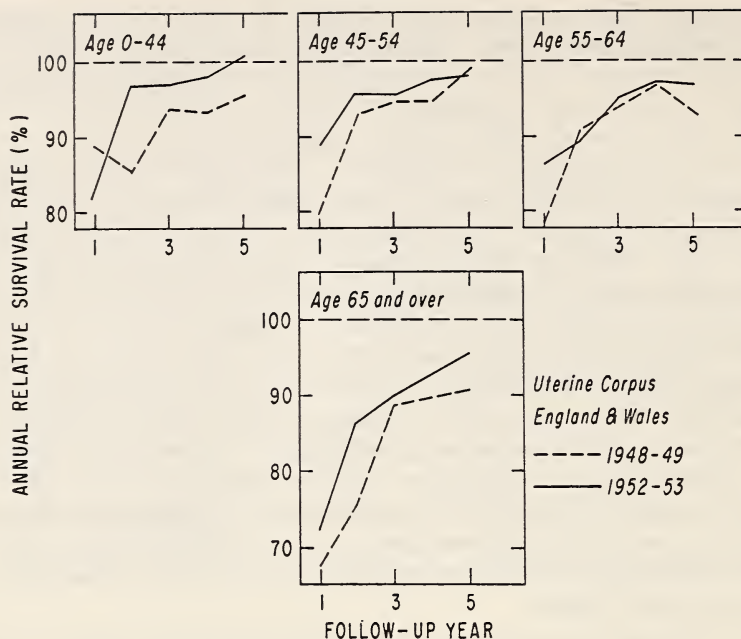
Table 6 and text-figure 6 show that the improvement in survival from the first to the second cohort was about equal in the four different age groups and was spread rather evenly over at least the first 5 years after diagnosis. Text-figure 6 is for England and Wales only, but similar patterns were noted in the reports on two cohorts from other areas.

TABLE 5.—Unadjusted and age-adjusted 5-year survival rates in various areas, cancer of the uterine corpus\*

	Five-year survival rate			
	Crude rate (%)	Age-adjusted rate † (%)	Relative rate (%)	Age-adjusted relative rate † (%)
Connecticut 1950-54	63.6	63.8	72.0	70.6
Denmark 1950-54	61.0	61.4	68.1	67.3
England and Wales 1952-53	58.3	59.6	66.2	66.0
Finland 1953-56	60.2	54.2	66.6	60.1
Norway 1953-56	52.2	53.1	58.8	57.7

\*All cases reported by hospitals, confirmed plus not confirmed, treated plus untreated.

†Age-adjusted by the direct method to age distribution of patients for all areas combined.



TEXT-FIGURE 6.—Relative survival rates for each follow-up year 0-5 years after diagnosis, by cohort, England and Wales, cancer of the uterine corpus (1).

(1) All cases reported by hospitals, confirmed plus not confirmed, treated plus untreated.

Although the absolute change in calculated survival rate was about equal in the various age groups, the relative change was greater at young ages than at old ages. For instance, in Connecticut the excess mortality of women aged 0-44 years was reduced by more than half, from 16.6 percent to 7.7 percent. The corresponding change at age 65 and over was 58.8 percent to 49.1 percent, a reduction of only about one sixth.

TABLE 6.—Change in 5-year relative survival rates, first cohort to second cohort, by age, cancer of the uterine corpus\*

Ages	Connecticut			Denmark			England and Wales		
	1945-49 (%)	1950-54 (%)	Change (%)	1945-49 (%)	1950-54 (%)	Change (%)	1948-49 (%)	1952-53 (%)	Change (%)
All combined	63.9	72.0	+8.1	61.3	68.1	+6.8	55.1	66.2	+11.1
0-44	83.4	92.3	+8.9	78.5	82.1	+3.6	63.2	76.0	+12.8
45-54	73.1	82.6	+9.5	74.7	79.1	+4.4	64.4	76.3	+11.9
55-64	66.7	73.0	+6.3	54.5	69.5	+15.0	59.7	68.6	+8.9
65 and over	41.2	50.9	+9.7	44.1	49.8	+5.7	37.2	50.5	+13.3

\*All cases reported by hospitals, confirmed plus not confirmed, treated plus untreated.

## Survival and Stage of Corpus Cancer

The difficulties of determining the stage of corpus cancer have already been mentioned. Because of these difficulties, it is hazardous to make comparisons of results by stage in various areas. However, within any area one can compare the results reported for localized tumors with those for more advanced tumors (table 7 and text-fig. 7). In each area, the "localized" group started with good survival rates, but these showed relatively little improvement with time. This means that the patient with a localized corpus cancer faced almost the same probability of death in the third, fourth, or fifth year as she did in the first year after the diagnosis of cancer. In contrast, patients with "not localized" tumors had low survival rates in the first year or two, but these rapidly rose toward the level of survival for patients with localized tumors. In three areas, Denmark, Connecticut, and England and Wales, there is a suggestion that survival, and hence, of course, mortality, was about equal in the two stage groups after 5 to 7 years. Thus, if corpus cancer patients with advanced tumors survived the first 5 to 7 years after diagnosis and treatment, their survival in subsequent years was no worse than that of patients originally reported to have localized tumors.

This similarity in late mortality rates between patients with localized tumors and those with "not localized" tumors may be of recent origin. Data for the earlier cohort (table 7) show a much greater excess mortality in the 5-10 year period among patients with "not localized" tumors than among those with localized tumors. Reasons for this decrease in the late mortality of corpus cancer patients are unknown. Improved treatment of the original cancer or more successful management of recurrences may be important factors.

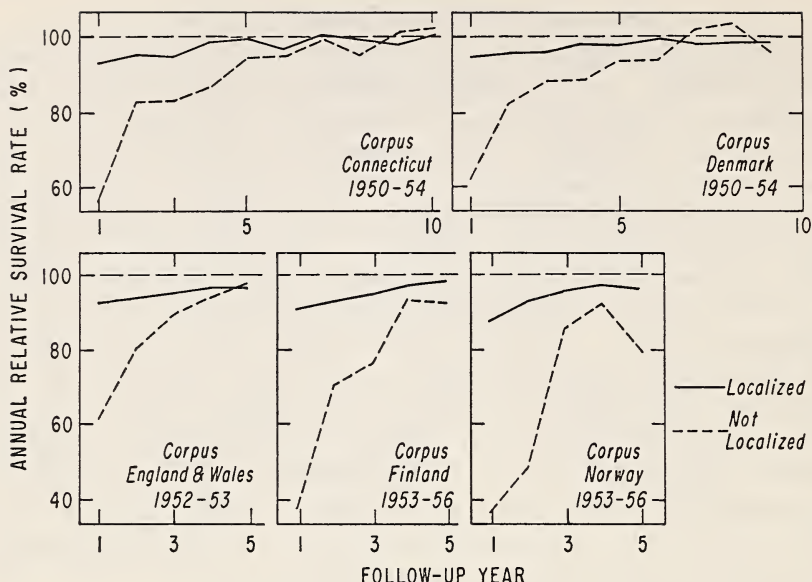
TABLE 7.—Relative survival rates by stage, 0-5 and 5-10 years after diagnosis, cancer of the uterine corpus\*

	Localized tumors		Not localized tumors	
	0-5 years (%)	5-10 years (%)	0-5 years (%)	5-10 years (%)
Connecticut 1945-49	77.0	94.3	27.9	78.3
1950-54	82.7	93.9	32.3	96.6
Denmark 1945-49	71.5	90.6	29.0	76.0
1950-54	78.9	91.1†	35.9	91.8†
England and Wales 1948-49	68.8	91.0	32.1	82.8
1952-53	78.8		42.8	
Finland 1953-56	77.3		19.5	
Norway 1953-56	72.9		11.2	

\*All cases reported by hospitals, confirmed plus not confirmed, treated plus untreated.

†Five to 9 years only. No patients were followed through the 10th year.





TEXT-FIGURE 7.—Relative survival rates for each follow-up year 0-5 years after diagnosis, by stage of cancer, in various areas, cancer of the uterine corpus (1).

(1) All cases reported by hospitals, confirmed plus not confirmed, treated plus untreated.

### Survival and Treatment of Corpus Cancer Patients

Surgery alone, radiation alone, and combined surgery and radiation all have been widely used for treatment of corpus cancer. Table 8 shows the distribution by primary treatment of corpus cancer patients in the areas under study. Radiation was most popular in Denmark, surgery was reported most often in Connecticut, and combined therapy was more common than either radiation or surgery alone in Norway. In both Denmark and England, there was an increase from the first cohort to the second cohort in the proportion of cases treated surgically, with a corresponding decrease in the use of radiation alone.

Although all three treatment methods were widely used, they are usually applied to somewhat different groups of patients. In general, the surgeon treats the most favorable ones—young patients, in good health, with localized tumors—and leaves the rest for the radiologist to treat. Also, surgically treated patients who are in addition given radiation therapy (which often precedes the surgery) are in many instances those patients for whom surgery alone is thought to be insufficient for cure. One may therefore expect a regular decrease in survival rates of the patients going from surgical to combined to radiologic treatment, regardless of any dif-



TABLE 8.—Distribution of patients by primary treatment method\* in various areas and time periods, cancer of the uterine corpus†

	Total cases		Surgery only (%)	Surgery plus radiation (%)	Radiation only (%)	No treatment reported (%)
	Number	Percent				
Connecticut 1945-49	910	100	43	30	19	8
1950-54	1122	100	44	33	19	5
Denmark 1945-49	1033	100	26	15	52	7
1950-54	1318	100	36	17	41	5
England and Wales 1948-49	1142	100	36	20	34	10
1952-53	1935	100	46	24	23	7
Finland 1953-56	822	100	16	47	27	10
Norway 1953-56	675	100	17	54	14	16

\*Treatment given in the first course of medical care for cancer.

†All cases reported by hospitals, confirmed plus not confirmed.

ferences in the true merits of these various forms of therapy. Departures from this expected pattern may be worth careful study.

Table 9 shows that, although some of the differences between categories were small, this general pattern appeared in the data for England and Wales, Finland, France, and the U.S. Central registries which include the Connecticut series. In Denmark, patients receiving combined therapy had significantly poorer survival than those receiving either surgery or radiation alone. In Norway and in the U.S. Hospital registry series

TABLE 9.—Five-year relative survival rates by treatment and stage in various areas, cancer of the uterine corpus\*

	Surgery only (%)	Surgery plus radiation (%)	Radiation only (%)
All cases			
Denmark 1950-54	84.6	54.3	62.3
England and Wales 1952-53	79.6	75.2	43.0
Finland 1953-56	79.1	75.1	60.7
France 1950-54	75.1	53.3	36.5
Norway 1953-56	65.9	76.0	30.0
U.S. Central registries 1950-54	82.0	78.5	51.3
U.S. Hospital registries 1950-54	78.1	81.9	44.6
Localized tumors only			
Denmark 1950-54	92.2	63.7	72.3
England and Wales 1952-53	85.1	81.7	56.4
Finland 1953-56	86.8	79.8	71.0
France 1950-54	78.4	62.2	49.5
Norway 1953-56	75.3	81.0	44.2
U.S. Central registries 1950-54	90.1	89.2	66.4
U.S. Hospital registries 1950-54	91.3	92.8	65.4

\*All cases reported by hospitals, confirmed plus not confirmed.

(contributed by a group of University hospitals in the United States) patients treated with combined surgery and radiation had higher survival rates than those treated with either surgery or radiation alone. This pattern is observed for patients with localized tumors as well as for all stages combined. More detailed tables (not given here) show that the higher survival after combined treatment than after surgery alone appears in each age group in these two series.

One might expect that surgically treated patients with advanced tumors would more often receive radiotherapy in addition to their surgery than surgically treated patients with localized tumors. This was true in each series except in Finland, where there was no significant difference, and in Norway and the U.S. Hospitals (table 10), the same two series that had higher survival rates after combined therapy than after surgery alone. This suggests that the selection of more favorable patients for radiation in addition to surgery was the most important factor in the higher survival of these patients in Norway and the U.S. Hospitals; reasons for selection in this way, rather than the reverse, should be determined.

Table 11 shows the relationship between treatment and survival in the period 5-10 years after diagnosis. With two exceptions in the "surgery only" group, survival remained below normal levels through this interval. Also, survival in the 5-10 year interval was in general somewhat lower for patients treated by radiation only than for those treated surgically, with or without radiation. This could be due to one or a combination of several factors, including selection of poor-risk patients for one form of treatment rather than another, differences in patient age or other important factors between the treatment groups, or deleterious effects of treatment directly affecting survival several years later. A previous study of Connecticut material for earlier years (6) suggested that radiation therapy for corpus cancer with the uterus left *in situ* was associated with an unusually high rate of recurrence and metastasis for at least 20 years after treatment. This finding should be checked, preferably in an area

TABLE 10.—Percent of surgically treated patients who also had radiotherapy, cancer of the uterine corpus\*

	All patients (%)	Reported as localized tumors (%)	Reported as not localized tumors (%)
Denmark 1950-54	32	28	48
England and Wales 1952-53	34	31	40
Finland 1953-56	74	74	75
France 1950-54	37	33	57
Norway 1953-56	76	78	75
U.S. Central registries 1950-54	44	43	49
U.S. Hospital registries 1950-54	70	72	65

\*All cases reported by hospitals confirmed plus not confirmed.

TABLE 11.—Relative survival rates for the period 5–10 years after diagnosis, in various areas, by treatment,\* cancer of the uterine corpus†

	Surgery only	Surgery plus radiation	Radiation only
Denmark 1945–49	97.9	76.9	84.2
1950–54	96.6‡	91.6‡	83.4‡
England and Wales 1948–49	94.1	94.6	72.8
U.S. Central registries 1945–49	95.5	90.5	83.2
1950–54	102.4	95.1	90.5
U.S. Hospital registries 1945–49	100.7	87.5	87.6
1950–54	85.8	99.5	97.8

\*Treatment given in the first course of medical cure for cancer.

†All cases reported by hospitals confirmed plus not confirmed.

‡Five to 9 years only. No patients were followed through the 10th year.

such as Denmark, where radiation alone is much more often used for endometrial cancer than in Connecticut.

### Sarcomas of the Uterine Corpus

Survival rates discussed thus far are for all histologic types of corpus cancers combined, including those not microscopically confirmed, but they are very close to those for adenocarcinoma alone. Survival rates for corpus sarcomas are somewhat different. Table 12 gives the total number of sarcomas for the registers supplying this information with relative survival rates in the 0–5 year and 5–9 year intervals. Carcinosarcomas are included. The proportion of corpus sarcomas relative to the total number of corpus tumors examined microscopically varied from 2 percent in the English series to 11 percent in Finland. It is not clear whether this wide variation is due to reporting artifacts, differing criteria of malignancy, or genuine differences from one area to another in the relative incidence of various forms of corpus cancer.

TABLE 12.—Numbers of cases and relative survival rates in various areas, sarcomas of the uterine corpus\*

	Number of patients	Percent of all corpus cancer reported as sarcoma	Relative survival rate	
			0–5 years (%)	5–9 years† (%)
England and Wales 1952–53	39	2.0	52.6	
Finland 1953–56	94	11.4	64.7	
France 1950–54	19	3.4	30.3	
Norway 1953–56	62	9.2	27.3	
U.S. Central registries 1950–54	137	5.7	48.3	94.9
U.S. Hospital registries 1950–54	18	3.3	40.9	85.6

\*All microscopically confirmed cases reported by hospitals, treated plus untreated.

†Five to 9 years only. No patients were followed through the 10th year.



Several features of the survival rates for corpus sarcomas merit brief comment. Except in Finland, these patients had appreciably lower survival than that reported for other types of corpus tumors, which are predominantly adenocarcinomas. The large Finnish group of sarcoma patients had survival rates as good as those for other patients with corpus tumors in Finland and considerably better than any other group of sarcoma patients. The reason for this is unknown, but it may be the result of including as cancer some borderline tumors that would be classified as leiomyomas elsewhere.

The lowest reported survival rate for corpus sarcomas was observed in Norway, which also had the lowest rate for corpus cancers of all histologic types combined. The limited figures from the United States suggest that sarcomas as well as adenocarcinomas are associated with elevated mortality rates in the 5–10 year interval. Further study of the survival of patients with corpus sarcomas would require more detailed information on reporting practices and pathologic criteria of malignancy.

## CERVICAL CANCER

The sources of data in the End Results tabulations and the errors which may be in them have been discussed. Here, as in the previous section on corpus cancer, most of the discussion will be confined to relative survival rates in five areas with complete or representative reporting of all known patients with cervical cancer—Connecticut, Denmark, England and Wales, Finland, and Norway.

### Geographic Variation in Survival of Cervical Cancer Patients

Text-figure 8 shows cumulative relative survival rates over the first few years after the diagnosis of cancer. There is wide variation in the reported relative survival rates, from 42 percent surviving at 5 years in England

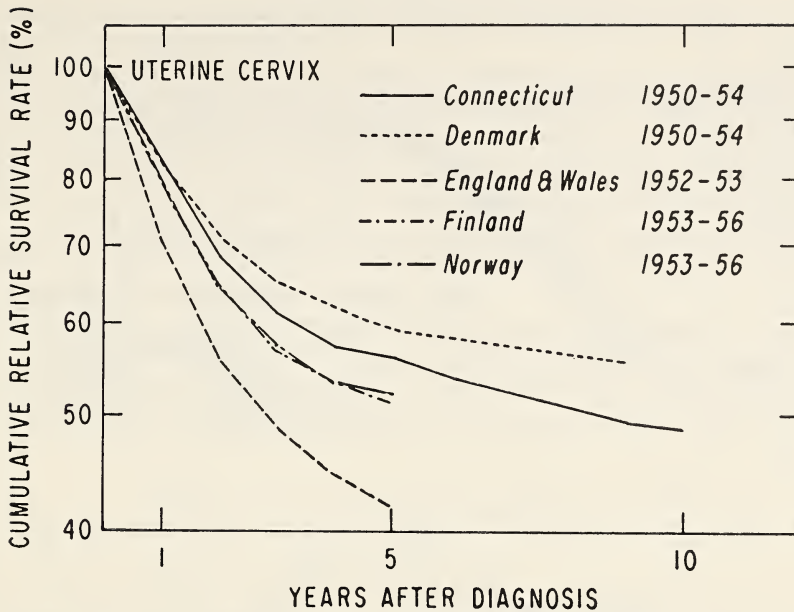
TABLE 13.—Unadjusted and age-adjusted 5-year survival rates in various areas, cancer of the uterine cervix\*

	Five-year survival rate			
	Crude rate (%)	Age-adjusted crude rate† (%)	Relative rate (%)	Age-adjusted relative rate† (%)
Connecticut	52.3	51.6	56.3	55.2
Denmark	56.4	54.0	59.8	57.5
England and Wales	38.1	39.1	42.0	42.1
Finland	47.9	46.7	51.4	50.3
Norway	49.0	48.2	52.0	51.4

\*All cases reported by hospitals, confirmed plus not confirmed, treated plus untreated.

†Age-adjusted by the direct method to age distribution of patients for all areas combined.





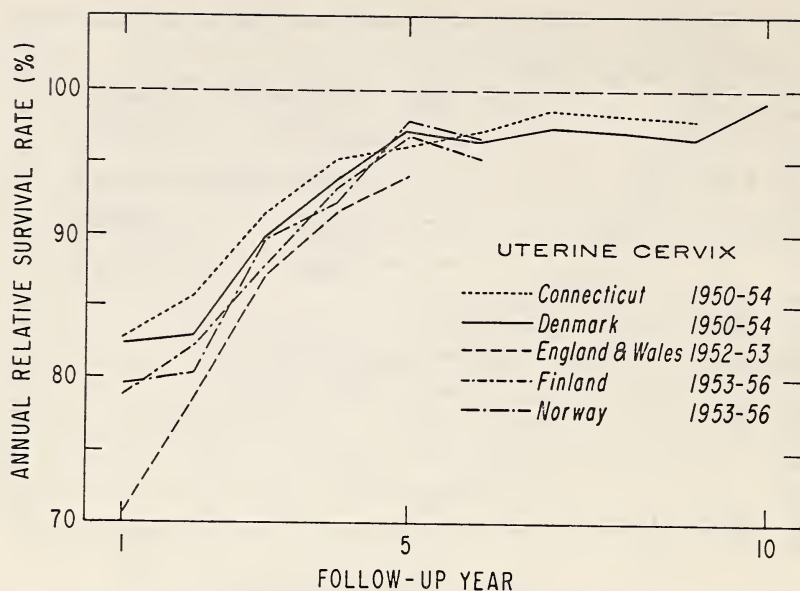
TEXT-FIGURE 8.—Relative survival rates 0-10 years after diagnosis, in various areas, cancer of the uterine cervix (1).

(1) All cases reported by hospitals, confirmed plus not confirmed, treated plus untreated.

and Wales to 60 percent in Denmark. Rates for the other three countries are closer to those for Denmark than to those for England and Wales. Age adjustment of the survival rates (table 13), similar to that for corpus cancer (table 5), does not change this pattern significantly.

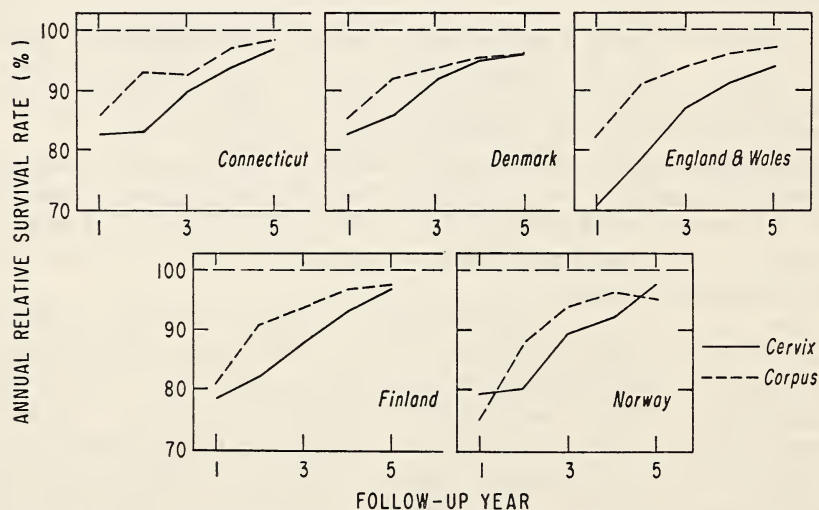
Text-figure 9 gives relative survival rates in the first ten 1-year intervals after the diagnosis of cancer. Survival was highest in Denmark for the first 4 years and lowest in England for at least the first 5 years. It is interesting that in Connecticut and Norway survival rates rose very little from the first to the second year.

The over-all pattern of survival of cervical cancer patients resembles that for corpus cancer except that it is somewhat lower. For both sites and in each of the five areas, survival rates were relatively low in the first year, but with time climbed toward "normal" survival levels. However, none of the survival rates did in fact reach normal levels even after as long as 10 years. A separate study of Connecticut patients (7) from earlier years showed that for cervical cancer, as for corpus cancer, the excess risk of death seems to persist as long as the patients are followed—certainly for at least 20 years. The Connecticut study also showed that the excess mortality of cervical cancer patients was largely or entirely due to late recurrences or metastases from the cervix, and that, in contrast



TEXT-FIGURE 9.—Relative survival rates for each follow-up year 0-10 years after diagnosis, in various areas, cancer of the uterine cervix (1).

(1) All cases reported by hospitals, confirmed plus not confirmed, treated plus untreated.



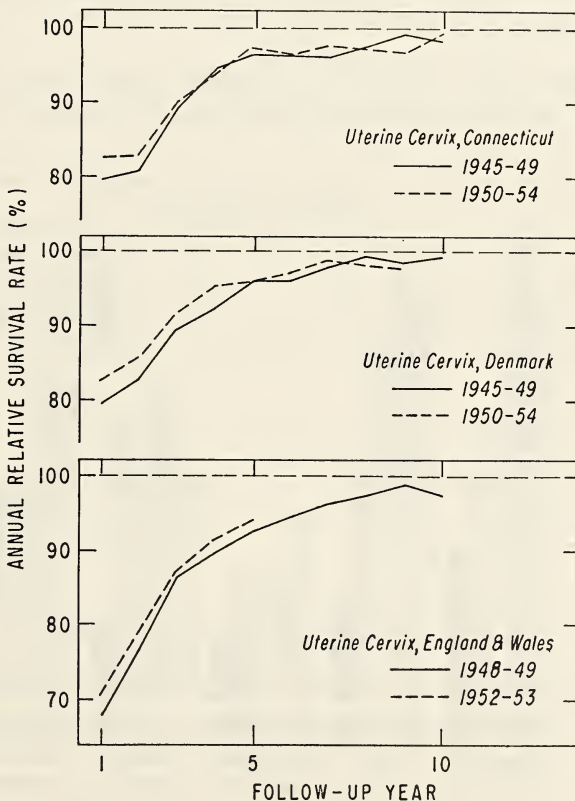
TEXT-FIGURE 10.—Relative survival rates for each follow-up year 0-5 years after diagnosis, in various areas, cancer of the uterine cervix and corpus (1).

(1) All cases reported by hospitals, confirmed plus not confirmed, treated plus untreated.

to corpus, it was not related to the primary treatment given many years earlier for the original cancer.

Text-figure 10 directly contrasts these interval survival rates for cervix with the corresponding survival rates for corpus cancer. With the exception of the first and fifth year in Norway, survival of corpus cancer patients was somewhat better in each area and in each of the 5 follow-up intervals; this was especially true in the second year after the diagnosis of cancer. In England and Wales, interval survival rates for cervical cancer remained well below those for corpus cancer, although the lines approached each other in the other four areas.

Survival of cervical cancer patients improved significantly from the first cohort to the second. Text-figure 11 shows interval survival rates in the three areas for which we have data from earlier years. In Connecticut and Denmark, at least, the improvement in survival has come mainly from



TEXT-FIGURE 11.—Relative survival rates for each follow-up year 0-10 years after diagnosis, in various areas and time periods, cancer of the uterine cervix (1).

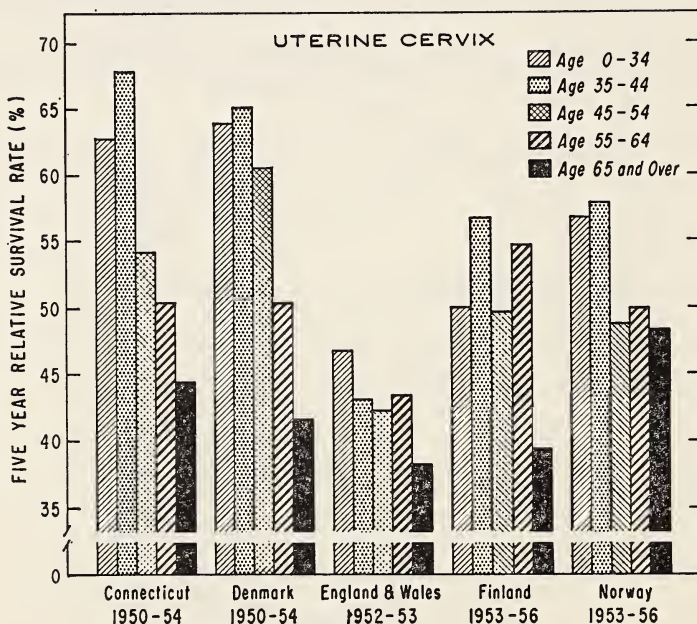
(1) All cases reported by hospitals, confirmed plus not confirmed, treated plus untreated.

reducing mortality in the first 2 to 4 years after diagnosis with little or no reduction in the excess mortality of patients living longer than 4 years. This suggests that in these two areas late recurrences and metastases from cervical cancer are still as common as they used to be. Recent survival data for English patients in the period 5–10 years after diagnosis are not yet available.

### Survival and Age of the Cervical Cancer Patients

There is a correlation between the age of cervical cancer patients and their prospects of survival, shown in text-figure 12, but this correlation is not as great as that observed for corpus cancer. Patients under 35 generally had somewhat lower survival than those aged 35–44, but further increases in age were accompanied by a decline in survival even after adjustment for “expected” mortality. Survival rates for England and Wales are lower than for any other area in each of the 5 age groups tabulated.

More detailed tables show that this correlation between age and survival is mostly or entirely due to a higher proportion of advanced tumors



TEXT-FIGURE 12.—Five-year relative survival rates by age at diagnosis of cancer, in various areas, cancer of the uterine cervix (1).

(1) All cases reported by hospitals, confirmed plus not confirmed, treated plus untreated.



TABLE 14.—Change in 5-year relative survival rates, first cohort to second cohort, by age, cancer of the uterine cervix\*

Ages	Connecticut			Denmark			England and Wales		
	1945- 49 (%)	1950- 54 (%)	Change (%)	1945- 49 (%)	1950- 54 (%)	Change (%)	1948- 49 (%)	1952- 53 (%)	Change (%)
All com- bined	52.3	56.3	+4.0	52.8	59.8	+7.0	37.6	42.0	+4.4
0-34	61.2	62.7	+1.5	53.6	63.8	+10.2	44.2	46.6	+2.4
35-44	62.0	67.7	+5.7	57.0	65.0	+8.0	40.9	42.9	+2.0
45-54	58.1	54.2	-3.9	54.4	60.5	+6.1	35.5	42.1	+6.6
55-64	46.3	50.4	+4.1	48.9	57.3	+8.4	39.2	43.1	+3.9
65 and over	31.0	44.4	+13.4	41.2	41.7	+0.5	34.2	38.0	+3.8

\*All cases reported by hospitals, confirmed plus not confirmed, treated plus untreated.

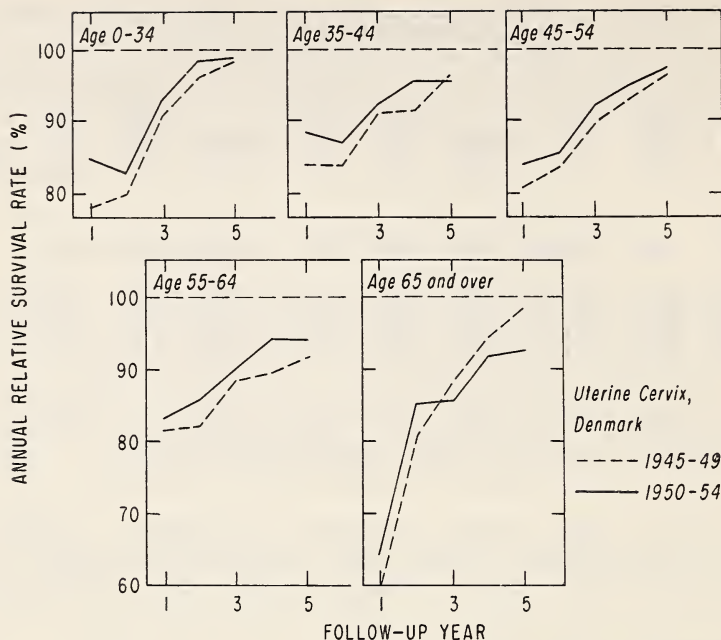
among older women. When comparisons are limited to patients with localized or not localized tumors alone, relative survival rates for older women are no lower than for younger women. This is in contrast to corpus cancer, which shows a strong correlation between age and survival, which does not depend on tumor stage.

Table 14 shows how the survival of patients in specific age groups has changed in the various areas. There seems to have been relatively uniform improvement in prognosis for each age group, when allowance is made for the small numbers of patients in some age categories. The improvement was on the whole greater in Denmark than in either Connecticut or England and Wales.

Text-figure 13 gives a more detailed picture of the change in age-specific survival rates in Denmark. Except at age 65 and older, the improvement generally extended over the full 5-year follow-up period. Figures for Connecticut and for England and Wales, not given here, show a similar but less consistent pattern.

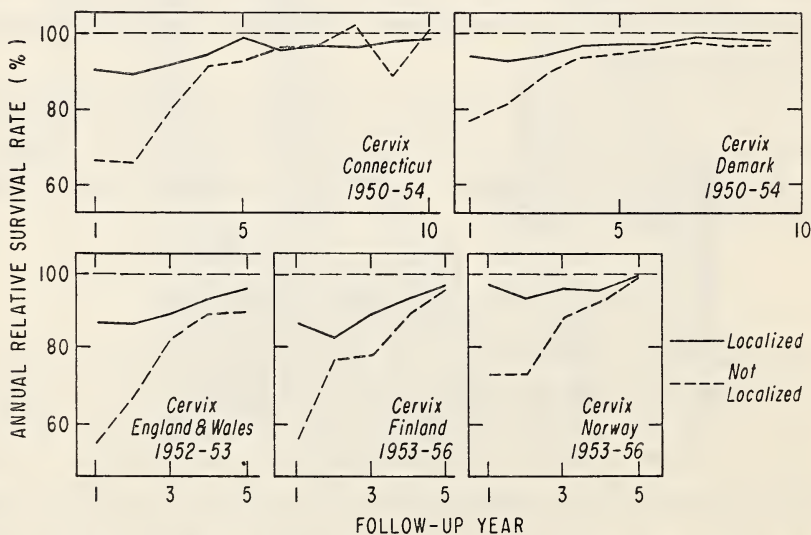
### Survival and Stage of Cervical Cancer

The difficulty of determining stage is as great for cervical cancer as for corpus cancer. In the absence of assured uniformity in the definition of stage and application of agreed principles, comparisons between various countries or between different time periods are hazardous. However, it is permissible to compare the survival of patients with localized tumors with that of patients with more advanced tumors in the same geographic area and the same time period. Text-figure 14 shows interval survival rates by stage in the more recent cohort. Patients with



TEXT-FIGURE 13.—Relative survival rates for each follow-up year 0-5 years after diagnosis, by cohort, Denmark, cancer of the uterine cervix (1).

(1) All cases reported by hospitals, confirmed plus not confirmed, treated plus untreated.



TEXT-FIGURE 14.—Relative survival rates for each follow-up year 0-5 years after diagnosis, by stage of cancer, in various areas, cancer of the uterine cervix (1).

(1) All cases reported by hospitals, confirmed plus not confirmed, treated plus untreated.

TABLE 15.—Relative survival rates by stage, 0-5 and 5-10 years after diagnosis, cancer of the uterine cervix\*

	Localized tumors		Not localized tumors	
	0-5 years (%)	5-10 years (%)	0-5 years (%)	5-10 years (%)
Connecticut 1945-49	64.8	89.7	29.8	80.8
1950-54	70.4	86.4	31.0	87.9
Denmark 1945-49	71.9	93.4	47.6	89.2
1950-54	78.3	94.4 †	50.3	90.6 †
England and Wales 1948-49	55.1	87.3	21.8	81.7
1952-53	59.4		24.2	
Finland 1953-56	60.3		29.8	
Norway 1953-56	78.7		41.6	

\*All cases reported by hospitals, confirmed plus not confirmed, treated plus untreated.

†Five to 9 years. No patients were followed through the 10th year.

advanced cervical tumors had much lower survival than those with localized tumors in the first 2 years. The difference was much smaller in later years but, except in the recent cohort in Connecticut, did not completely disappear (table 15). More detailed tables show that with minor exceptions this pattern holds in all age groups.

### Survival and Treatment of Cervical Cancer Patients

There is an active controversy over the relative merits of surgery and radiation in the primary treatment of cervical cancer. There have been repeated and persuasively argued claims that surgery is superior to radiation, that radiation is superior to surgery, and that a combined course of surgery and radiation is superior to either one alone. It is not possible to resolve this question with the data at hand. However, it is possible to describe the use of various modes of therapy at various times and places.

Table 16 shows the proportions of patients in each of the three main treatment categories. Radiation alone was the most common form of treatment. More detailed tables show that this was true in all age groups and for both stage groups except among young Norwegian patients with localized cervical cancer, for whom the usual treatment was surgery plus radiation.

Meaningful comparison of survival rates in various treatment categories is complicated by the universal, and necessary, selection for surgery of patients with better-than-average prognoses. This is naturally reflected by higher survival rates of surgically treated patients in each area and hospital group studied, including France and the U.S. Hospital group

TABLE 16.—Distribution of patients by primary treatment method\* in various areas and time periods, cancer of the uterine cervix†

	Total cases		Surgery only (%)	Surgery plus radiation (%)	Radiation only (%)	No treatment reported (%)
	Number	Percent				
Connecticut 1945-49	1077	100	13	12	68	7
1950-54	1069	100	19	12	65	4
Denmark 1945-49	2979	100	2	5	87	7
1950-54	3568	100	8	8	78	6
England and Wales 1948-49	5396	100	4	9	80	8
1952-53	5580	100	6	12	75	7
Finland 1953-56	1387	100	3	10	81	6
Norway 1953-56	1273	100	2	17	78	4

\*Treatment given in the first course of medical care for cancer.

†All cases reported by hospitals, confirmed plus not confirmed.

(table 17). However, even the surgically treated patients, mostly patients with localized tumors and in good general health, did not attain normal survival rates within the 5-10 year period after the diagnosis and treatment of cancer (table 18). This is yet one more indication of the very long-lasting effects of malignant neoplasms on health and life, even when the patient is in good general health and receives apparently adequate treatment for a localized cancer.

TABLE 17.—Five-year relative survival rates by treatment and stage in various areas, cancer of the uterine cervix\*

	Surgery only (%)	Surgery plus radiation (%)	Radiation only (%)
All cases			
Denmark 1950-54	80.0	37.9	60.9
England and Wales 1952-53	62.0	55.6	41.2
Finland 1953-56	60.1	64.5	51.5
France 1950-54	58.9	58.6	47.3
Norway 1953-56	80.6	78.0	47.3
U.S. Central registries 1950-54	85.0	65.1	54.7
U.S. Hospital registries 1950-54	77.6	56.5	56.0
Localized tumors only			
Denmark 1950-54	91.4	55.6	78.2
England and Wales 1952-53	77.9	65.8	56.3
Finland 1953-56	66.1	68.6	59.2
France 1950-54	70.2	75.2	65.6
Norway 1953-56	†	86.6	70.2
U.S. Central registries 1950-54	92.3	78.1	71.9
U.S. Hospital registries 1950-54	93.9	76.4	77.0

\*All cases reported by hospitals, confirmed plus not confirmed.

†No cases followed for 5 years.



TABLE 18.—Relative survival rates for the period 5–10 years after diagnosis, in various areas, by treatment,\* cancer of the uterine cervix†

	Surgery only	Surgery plus radiation	Radiation only
Denmark 1945–49	97. 7	82. 7	91. 2
1950–54	96. 6‡	81. 6‡	92. 2‡
England and Wales 1948–49	92. 0	93. 3	84. 3
U.S. Central registries 1945–49	94. 3	94. 9	85. 3
1950–54	90. 1	88. 6	86. 8
U.S. Hospital registries 1945–49	95. 3	82. 6	87. 7
1950–54	95. 1‡	98. 1‡	87. 8

\*Treatment given in the first course of medical care for cancer.

†All cases reported by hospitals, confirmed plus not confirmed.

‡Five to 9 years only. No patients were followed through the 10th year.

### Survival of Cervical Cancer Patients in England and Wales

For almost every category of cervical cancer patients, the survival rates reported by England and Wales are lower than those in any of the other study areas. In contrast the prognoses of English patients with cancer of the uterine corpus are about average when compared with those in the other areas. This contrast is the most striking feature of these data. There are at least four explanations to be considered for the low survival of cervical cancer patients in England.

First, the English data cover only about half of all the patients in the country. Do good-risk patients have a higher chance of escaping the reporting network than poor-risk patients? This is possible but unlikely: Reporting of patients treated by irradiation is thought to be more complete than reporting of those treated by surgery only, and radiation is generally the treatment of choice for cervical cancer in England as well as elsewhere; it is difficult to think of reporting biases that would depress cervical cancer survival rates so much without depressing corpus cancer survival rates significantly; and the low survival of cervical cancer patients has been noted in areas of England, such as the Southwestern Hospital Board Region, where reporting is essentially complete.

A second possibility is that many cervical cancer patients in England receive inadequate treatment. Against this hypothesis is the high respect accorded throughout the world to English physicians and English medical training and, more important, the absence of unusually low survival rates for most other sites of cancer, including corpus. However, poor treatment on a wide scale remains a possibility and cannot be dismissed by the evidence at hand.

Is cervical cancer in England different in some way from cervical cancer in other countries? Incidence rates for cervical cancer are not

different from those for other areas in Western Europe and North America, and there have been no reports of morphologic differences between cervical cancers in England and those found elsewhere. One study specifically designed to look for such differences has not yet revealed any microscopic features characteristic of English tumors which would explain the low survival rates of these patients. Dr. Thomas will discuss this work later in this Symposium (7).

A fourth possible explanation for the low survival rates of cervical cancer patients in England and Wales is that there is an unusually high proportion of patients with advanced tumors. A recent review of records for a representative series of about 200 cervical cancer patients living in or near one middle-sized English city showed an unusually high proportion of patients with a long history of symptoms and large, inoperable tumors (5). This delay in seeking medical consultation for cervical cancer was attributed by local physicians and cancer registry personnel to a combination of many things: ignorance of the population about the basic facts of cancer, widespread stoicism and apathy, difficulty in transportation to and from centralized facilities for diagnosis and treatment, the stigma which is still popularly attached to cancer in England, a Victorian aversion to discussing the common symptoms of cervical cancer even with physicians, and the active opposition of some parts of the medical profession to any efforts at public education about cancer. Thus there is some reason to believe that cervical cancer patients present themselves for treatment at a relatively late stage in the disease; this would explain their low survival rates in all the various categories of age, stage, treatment, etc. There is, however, one serious weakness in this argument—the survival rates of corpus cancer patients are near those observed in other areas. It is difficult to believe that cervical cancer patients in England would delay consulting a physician appreciably longer than those in other areas, but that corpus cancer patients, with identical signs and symptoms in a high proportion of cases, would consult physicians as promptly as they do elsewhere.

In attempting to explain the unusually and consistently low survival rates of cervical cancer patients in England and Wales, some clues might come from a more detailed comparison of the characteristics of English patients (including the extent of their cancers) with those of patients in a high-survival area such as Connecticut or Denmark. A careful and detailed review of original case records with interview of a sample of patients could lead to significant discoveries about the detection and treatment of cancer, and might result in further reduction in cervical cancer mortality in both low-survival and high-survival areas. If such a study does not adequately explain the low survival of cervical cancer patients

TABLE 19.—Numbers of cases and relative survival rates in various areas, adenocarcinomas of the uterine cervix\*

	Number of patients	Percent of all cervical cancer reported as adenocarcinoma	Relative survival rate	
			0-5 years (%)	5-10 years (%)
Denmark 1950-54	124	3.5	50.2	81.4†
Finland 1953-56	85	6.1	49.2	
France 1950-54	255	6.7	46.4	90.7
Norway 1953-56	77	6.0	43.2	
U.S. Central registries 1950-54	336	9.1	62.8	88.1†
U.S. Hospital registries 1950-54	92	5.7	44.3	94.3†

\*All microscopically confirmed cases reported by hospitals, treated plus untreated.

†Five to 9 years only. No patients were followed through the 10th year.

in England, some evaluation of the quality of treatment, especially radiotherapy, would be helpful.

#### Adenocarcinomas of the Uterine Cervix

The results discussed thus far for all malignant cervical tumors are essentially those for squamous cell carcinomas alone. For adenocarcinomas of the cervix the picture is somewhat different. Table 19 shows the number of cervical adenocarcinomas reported in various areas, with relative survival rates in the 0-5 and 5-10 year intervals. Unfortunately, these data are not available for England and Wales. The proportion of cervical tumors reported as adenocarcinomas varied from 3.5 percent in Denmark to 9.1 percent in the U.S. Central registries.

Except in the U.S. Central registries, survival of these patients in the 0-5 year period was lower than that of patients with other forms of cervical cancer. After 5 years, survival rates for adenocarcinomas were about the same as those for other types of cervical cancer. Both groups showed a significant excess of mortality above that "expected" from mortality rates in the general population.

The 366 patients reported by U.S. Central registries had a 5-year survival rate well above that reported by any other group, while the U.S. Hospitals reported nearly the lowest survival rate. This discrepancy is rather surprising, but may be the result of selection of poor-risk patients for referral to treatment centers such as those in the U.S. Hospital category. There is some evidence for selective referral. In the U.S. Central registries, adenocarcinomas of the cervix were reported as localized distinctly more often than were other cervical tumors (61% vs 53%); in the U.S. Hospitals the proportions reported as localized in the two groups were nearly equal (43% vs 42%). Further study of cervical adenocarcinomas, as of corpus sarcomas, would require more detailed information on reporting practices and diagnostic criteria used in the various areas.



## SUMMARY AND CONCLUSIONS

The most important points revealed by the End Results tabulations for patients with cancer of the uterine cervix and corpus are the following:

1) There are large and significant differences from one area to another in the prognosis of patients with cancer of the cervix or corpus.

2) In each area, older patients have a much lower probability of surviving than younger patients, even after adjustment for the higher mortality of older persons from diseases other than cancer. For cervical cancer, but not for corpus, this correlation between age and survival can be explained by the higher proportion of advanced tumors among older women than among younger women.

3) Survival rates of patients with cancer of the cervix or corpus remain below "expected" levels for at least 10 years after diagnosis and treatment, regardless of the age of the patient, the stage of the cancer, the geographic area, the method of treatment, or the histologic type of the tumor.

4) For both sites of cancer, survival has improved in recent years. However, the improvement for cervical cancer was generally limited to the first few years after diagnosis; mortality from late recurrences and metastases of cervical cancer seems to have been reduced very little.

5) Cervical cancer patients in England and Wales have survival rates well below those in any other area studied. The poor survival of these patients is especially noteworthy because corpus cancer patients in England and Wales have survival rates near the average.

6) These data make clear the need for studying many problems in methodology, including international and local variations in the interpretation and application of tumor stage definitions, the extent of differences in diagnostic criteria for various types of tumors, and the effect on reported survival rates of differences in method of follow-up, calculation of rates, and definition of various categories of patients.

7) A partial list of problems for further study must include the following: reasons for the observed international differences in survival rates; factors causing patients to seek medical advice at an earlier or later stage of cancer; causes of the excess mortality among patients who had cervical or corpus cancer 5 to 10 years earlier; and relationships between this late excess mortality and the treatment originally given for cancer.

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## Comparison of the Pathology of Cervical Cancer in Connecticut and the Southwest Region of England<sup>1</sup>

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GEOGRAPHIC variation in the incidence of cancer of the cervix and in the survival of cervical cancer patients has been known for decades. With the recent growth of large-scale cancer registry systems it has become possible to study in detail these variations in incidence and survival from one area to another. Table 1 shows the differences in the data reported from two central registries with essentially complete reporting of all cervical cancer patients in the corresponding populations. The Connecticut Tumor Registry, prototype of many of the population-based registries now in existence, carries incidence and survival data on all known cancer patients in a population of over 2 million persons; this population gives rise to over 200 new cases of cervical cancer each year. The cancer registry system operated by the Southwestern Hospital Board Region of England and Wales is similar in many ways but somewhat larger in the population covered and in the number of new cases reported per year.

The incidence rate of 20.2 for Connecticut is appreciably higher than the rate, 14.6, for the Southwest Region. Also the 5-year survival rate is much higher in Connecticut than in England—52 percent as contrasted to 36 percent. At least part of this difference in survival is due to a difference in stage—in Connecticut, approximately half of the cervical

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<sup>1</sup> Presented in part by Dr. A. D. Thomson at the VIII International Cancer Congress, Moscow, USSR, July 22–28, 1962.

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<sup>6</sup> National Institutes of Health, Public Health Service, U.S. Department of Health, Education, and Welfare.

TABLE 1.—Cervical cancer in Connecticut and the Southwestern Hospital Board Region of England

	Connecticut	Southwest Region
Annual incidence per 100,000,* cervical cancer	20. 2†	14. 6‡
Cervix-corpora ratio§	0. 75	0. 82
5-year survival rate, cervical cancer	52. 3%	35. 5%

\* Age adjusted to Connecticut population, 1950.

† Cases diagnosed 1947-51.

‡ Cases diagnosed 1954-57.

§ Cases diagnosed 1957-58.

|| Cases diagnosed 1950-54.

Source: Unpublished tabulation from the tumor registries in Connecticut and the Southwestern Hospital Board Region of England and Wales.

cancer patients are reported as localized (stage I) at the time of diagnosis whereas only 1 in 4 are reported as localized in the Southwest Region of England. However, even when comparisons are limited to specific stage groups, the Connecticut patients had better survival rates than those in England. The cervix-corpora ratios were similar in the two areas and were much lower than those usually reported.

In 1959 the late Dr. Alan McKenzie of the General Registry Office of England and Wales visited Connecticut to study these differences. As a result of his visit it was decided to undertake a combined pathological and statistical survey of cervical cancer in the two areas. It was agreed that two pathologists, one from the United States and one from England, would together visit all hospitals in each area and review histological sections of all cases of carcinoma of the cervix and of the corpus that were first diagnosed in Connecticut or in the Southwest Region during 1957 and 1958.

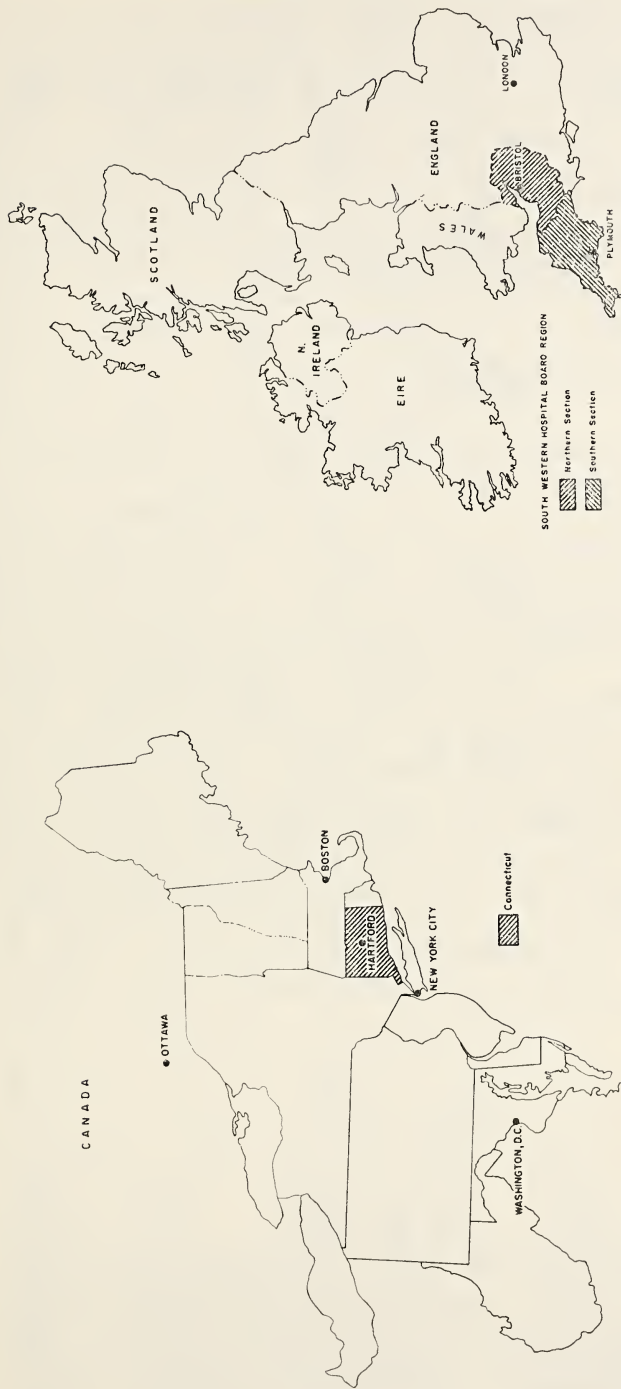
Text-figure 1 shows the areas covered by the survey. The two regions are approximately the same size and are similar in many other characteristics, such as population density, climate, and geography. The English region is divided into a northern and southern section for administrative purposes.

The first purpose of the survey was to re-examine slides on all types of cancer of the uterus and to verify the original diagnosis. For invasive squamous cell carcinomas of the cervix, more detailed information was recorded on a protocol sheet.

## DISTRIBUTION OF CASES OF UTERINE CANCER REVIEWED

Table 2 shows the distribution of all cases reported by the central registries, the number of cases added or deleted, and the histologic type of each tumor that was reviewed microscopically. There were 1,982 cases that met the four study criteria: 1) that the tumor be primary in the





TEXT-FIGURE 1.—Cancer registration areas, Connecticut and Southwest Region of England.

TABLE 2.—Distribution of cases of uterine cancer reviewed\*

	Connecticut		Southwest Region, England		Total
	Cervix 428	Corpus 554	Cervix 477	Corpus 566	
Reported by central registries					2025
Cases deleted	-33	-33	-15	-12	-93
Not considered malignant on microscopic review					
Registration errors	16	18	6	3	43
Not malignant, reported by error	17	15	9	9	50
Not primary in uterus	8	9	5	2	24
Not 1957 or 1958 diagnosis	3	5	0	2	10
Duplicate records	3	0	4	5	12
Cases added	+6	+12	+10	0	4
Number of cases meeting study criteria	401	533	472	576	1982
Cases not reviewed microscopically					
No biopsy taken	63	52	73	96	284
Admitted to hospitals	18	25	64	84	191
Death certificate report only	1	5		19	49
Biopsy taken	45	27	9	12	142
Malignant tumor histologically reviewed					
Squamous cell carcinoma	338	481	399	480	93
Suitable for detailed study	324	0	382	0	706
Not suitable	277	—	359	—	636
Adenocarcinoma	47	23			70
Leiomyosarcoma	13	438	13	443	907
Stromal sarcoma	0	13	0	17	30
Carcinoma	0	1	0	1	2
Undifferentiated sarcoma	1	8	0	3	12
Choriocarcinoma	0	6	0	1	7
Choriocarcinoma <i>desruens</i>	0	1	0	1	2
Anaplastic tumor	0	2	0	0	2
Reported as carcinoma <i>in situ</i>					
Meeting study criteria	255	10	12	14	30
Not meeting study criteria	91	4	9	1	104
	164	6	3	1	174

\*Cases tabulated according to site, determined by review of 1098 tumors re-examined microscopically; other cases tabulated according to site listed on central registry records.

uterine cervix or corpus; 2) that it be invasive; 3) that the patient be a resident of the study area at the time of diagnosis; and 4) that the diagnosis had first been made in 1957 or 1958. In addition, there were 278 cases of carcinoma *in situ* reported during the same 2 years.

Five hundred fifty-four patients in Connecticut and 566 in the Southwest Region of England were reported by the registries as having cancer of the corpus uteri, first diagnosed in 1957 and 1958. Thirty-three in Connecticut and 12 in the Southwest Region were deleted from the study. Twelve cases in Connecticut and 22 cases in the Southwest Region were added so the net totals for cancer of the corpus were 533 and 576 cases, respectively. The cases added, which were found on visits to the various hospitals, had not been recorded in the central cancer registries. Eighteen cases in Connecticut and 3 in England were not considered malignant on review and were also deleted.

Eighty-four cases in the Southwest Region and 25 cases in Connecticut could not be reviewed because there was no record that a biopsy had ever been taken. In addition, there were a few cases in each area with the initial diagnosis based on biopsy, but the histological sections were not available for review. This left 481 cancers of the corpus in Connecticut and 480 in England that were reviewed and met all study criteria. Most were adenocarcinomas but there were a few leiomyosarcomas, anaplastic tumors, and other varieties of malignant tumors.

In Connecticut the central registry had 428 cases of invasive cervical cancer listed for 1957 and 1958, and in the Southwest Region of England the registries had 477 invasive cancers of the cervix listed for the same 2 years. Sixteen cases in Connecticut and 6 in the Southwest Region were not considered malignant on review, and 17 cases and 9 cases in the two areas were deleted because of errors of registration.

Sixty-three of the 401 cases of invasive cancer of the cervix in Connecticut were not reviewed microscopically. The slides for 45 of these were not available and in 18 other cases the diagnosis had not been confirmed microscopically. Most of the latter cases were reported to the central registry on death certificates only. In the Southwest Region of England there were 64 patients whose diagnoses were never established by biopsy. Thus, the microscopic review was limited to 338 invasive cancers of the cervix in Connecticut and 399 in the Southwest Region of England. Most of these were invasive squamous cell carcinomas. There were 13 adenocarcinomas of the cervix in each area.

Tables 2 and 3 show the distribution of the 43 tumors that were originally reported as malignant but which were not considered malignant by the reviewing pathologists. For the cervix, 9 of the 21 cases initially diagnosed as "carcinoma *in situ* with early invasion" and 12 others (7 in Connecticut and 5 in England) initially diagnosed as squamous cell carcinoma often had some note or comment about possible or questionable invasion. These 21 were considered on review to be cases of hyperplasia,

TABLE 3.—Cases not considered malignant on microscopic review

Original diagnosis	Review diagnosis	Total	Connecticut	Southwest Region
Total, uterus		43	34	9
Cervix		21	16	5
Squamous cell carcinoma	Hyperplasia, metaplasia, etc.	12	7	5
Carcinoma <i>in situ</i> , early invasion	Squamous metaplasia, with gland replacement	9	9	—
Corpus		22	18	4
Adenocarcinoma	Atypical hyperplasia	12	8	4
Early carcinoma in endometrial polyp	Atypical hyperplasia	4	4	—
Leiomyosarcoma	Cellular leiomyoma	3	3	—
Fibrosarcoma	Cellular leiomyoma	3	3	—

metaplasia, or metaplasia with gland replacement. For corpus cancer, there were 12 cases in Connecticut and 4 in the Southwest Region with an initial diagnosis of "early adenocarcinoma" or "early carcinoma in an endometrial polyp," which on review were interpreted as hyperplasia or epithelial atypia. In addition, 6 other cases in Connecticut were originally diagnosed as leiomyosarcoma or fibrosarcoma, but were interpreted on review as cellular leiomyomas.

Regarding these 43 cases three points should be noted: 1) Many were recognized as difficult diagnostic problems both at the time of initial diagnosis and at review. Also, the reviewing pathologists often had biopsy or surgically removed material to examine, in addition to the material on which the diagnosis was initially based. 2) For this survey, it was desirable to use more strict criteria for the diagnosis of cancer than are usually applied in the day-to-day practice of pathology. This was done to avoid dilution of the groups of definite cancer cases with those of uncertain diagnosis. 3) These 43 cases were from a total group of 1,698 malignant, invasive cancers reviewed and therefore represent only 2.5 percent of that total.

### SQUAMOUS CELL CARCINOMA IN CONNECTICUT AND THE SOUTHWEST REGION OF ENGLAND

There were 324 invasive squamous cell carcinomas in Connecticut and 382 in the Southwest Region which were reviewed microscopically. Although the diagnosis of cancer could be verified for each of these cases, some of the histological sections were not adequate for detailed analysis because of necrosis, inadequate material, or for other reasons. There were 277 cases in Connecticut and 359 in the Southwest Region suitable for de-



## Protocol for squamous cell carcinoma

<i>Pattern:</i>	Solid	Fingers	Indeterminate			
<i>Cells:</i>	Squamous cells-----	25%	50%	75%	100%	
	Basal type cells-----	25%	50%	75%	100%	
<i>Differentiation:</i>	Differentiated		Average	Undifferentiated		
<i>Other changes:</i>						
Necrosis	None	Slight	Moderate	Marked		
Keratinous debris	None	Slight	Moderate	Marked		
Mitoses	0-4	5 or more				
Bizarre cells	Inconspicuous	Conspicuous				
<i>Stroma:</i>						
Eosinophils	Inconspicuous	Conspicuous				
Fibrosis	Inconspicuous	Conspicuous				
Plasma cells	Inconspicuous	Conspicuous				

tailed histological analysis. All were examined according to the above pre-arranged protocol.

Special attention was given to the pattern of the invading tumor, to the type of cell forming the tumor, and to other features such as necrosis, mitoses, bizarre cells in the tumor, and the amount and nature of the stromal reaction. After all these histological features had been noted, the degree of tumor differentiation was independently evaluated to determine the grade of malignancy. The tumors were divided into three categories which were designated differentiated, average, and undifferentiated. Table 4 shows that the results of this grading were very similar in the two areas.

An analysis of some of the other detailed histological features does suggest some variation in the characteristics of squamous cell carcinomas of the cervix in the two geographical areas, but it is not yet known whether these variations are real or whether they can be correlated with survival rates. A detailed analysis of these histological features and 5-year survival will be reported when information on 5-year survival is available.

*Carcinoma In Situ*

The principal purpose of this combined pathological and statistical study was to compare invasive squamous cell carcinoma of the cervix in Connecticut with that in the Southwest Region of England. Carcinoma

TABLE 4.—Differentiation of squamous cell carcinomas

	Number of cases	Differentiated (%)	Average (%)	Undifferentiated (%)
Connecticut	277	5	83	10
Southwest Region	359	6	83	11

*in situ* was included to determine some of the relationships between it and invasive carcinoma.

Many clinicians and pathologists in Connecticut have been active in the development of cytology clinics and in the use of cytologic methods for the early detection of carcinoma of the cervix. These cytologic studies followed by biopsy of the cervix in suspicious or positive cases have led to the diagnosis of many cases of carcinoma *in situ* as well as invasive cancer. By contrast, many British clinicians and pathologists, at least in the Southwest Region, have been reluctant to use cytologic methods extensively. Furthermore, pathologists in Britain have been less liberal than those in Connecticut in their definitions of criteria for the diagnosis of carcinoma *in situ*. These differences in attitude and practice between Connecticut and the Southwest Region are vividly reflected in the number of cases of carcinoma *in situ* reported in the two areas.

Table 2 shows that there were 255 cases of carcinoma *in situ* diagnosed in Connecticut in 1957 and 1958 and 12 cases in the Southwest Region. None of these 12 cases were actually listed in the central tumor registries in Bristol and Plymouth. They were found by a search of the files of pathology laboratories in the Southwest Region. In other words, the central registries did not have any specific information about cases of carcinoma *in situ*. The term was not even listed on their record forms.

There are numerous, almost imperceptible, histological gradations from normal cervical epithelium to the fully developed lesion of carcinoma *in situ* in which the entire epithelium is replaced by atypical, enlarged, hyperchromatic cells. Most of the disagreement about the diagnosis of carcinoma *in situ* centers around intermediate changes in the cervical epithelium. For the purposes of this review it was necessary to use rigid criteria for the diagnosis of carcinoma *in situ*. Also in this survey no case was accepted as carcinoma *in situ* if the epithelial change was present only in endocervical glands. This latter criterion was adopted because of the well-known difficulty of distinguishing the epithelial change of carcinoma *in situ* from the tip of a normal endocervical gland cut tangentially. In other words, all cases accepted as carcinoma *in situ* showed the typical epithelial change some place on the surface of the endocervix or exocervix.

Ninety-one of the 255 cases reported to the Central Registry in Connecticut met the rigid study criteria. The other 164 included many cases of epithelial atypia and other epithelial changes that are often diagnosed as carcinoma *in situ*. However, on review, many of these were thought to be over-diagnosed. Some were examples of squamous metaplasia, cervicitis, or regenerating epithelium over the base of a cervical ulceration. Others were examples of basal cell hyperplasia, a lesion diagnosed as carcinoma *in situ* by many pathologists. Each of the 91 patients accepted as having carcinoma *in situ* and all but 6 of the remaining 164 patients had had a hysterectomy. This will, of course, prevent observation of the development of these lesions. The average age of the 91 patients with

TABLE 5.—Histological features of uterine cervix adjacent to invasive squamous cell carcinoma

	Connecticut		Southwest Region	
Total cases of squamous cell carcinoma	277		359	
Adjacent cervix suitable for study	125		100	
Not remarkable	31	25%	33	33%
Glandular hyperplasia*	53	42%	43	43%
Squamous metaplasia*	26	21%	24	24%
Carcinoma <i>in situ</i> *	50	40%	22	22%

\*Some tumors had more than one of these characteristics.

carcinoma *in situ*, according to the study criteria, was 42.8 years and the average age of the 164 patients not meeting the criteria was 39.2 years. These may be compared with the average age of 53.5 years of patients with invasive cervical cancer.

Even though strict criteria were used for the diagnosis of carcinoma *in situ* there were nearly 10 times as many cases in Connecticut as in the Southwest Region of England. It is possible that there is indeed a difference in the incidence of carcinoma *in situ* among women in the two areas, but almost certainly the difference is not as great as 10 to 1. In fact, carcinoma *in situ* was seen adjacent to infiltrating squamous cell carcinoma in 22 percent of the English cases (table 5). However, the data presented in table 5 suggest that the lesion may be more frequent in Connecticut since it was observed in 40 percent of the patients with invasive squamous cell carcinoma.

## CONCLUSIONS

Although this study is not yet complete, some conclusions are already warranted.

1) Nearly every lesion that was diagnosed invasive cancer in Connecticut would also be considered invasive cancer in the Southwest Region of England and vice versa.

2) There was a striking similarity in the proportion of tumors classified as differentiated, average, or undifferentiated in the two regions. Thus there is probably no significant difference in the grade of malignancy of the cervical tumors.

3) Biopsy specimens in England were on the whole very large, and many of these were composed entirely of tumor tissue without any normal or uninvaded cervix. In Connecticut, it was possible to describe the changes in the adjacent, uninvaded cervical tissues in 125 (44%) of 277 cervical biopsies, but in the Southwest Region this could be done in only 100 (28%) of 359 biopsies. This suggests that cervical tumors were considerably larger at the time of diagnosis in the Southwest Region. This is also supported by the observation that approximately half of the cervical



cancer cases in Connecticut were reported as localized (stage I) at the time of diagnosis, whereas only 1 in 4 was reported as localized in the Southwest Region of England.

4) The Connecticut series included 11 cases of squamous cell carcinomas which were less than 0.5 cm in diameter but had definite evidence of invasion of the underlying cervical tissues. There was only 1 such case found in the Southwest Region. The 11 cases from Connecticut were all diagnosed initially by means of exfoliative cytology, while the single case from the Southwest Region was an incidental finding in a uterus removed for procidentia in which no malignancy was suspected.

5) It has been suggested that the high incidence rate and the high 5-year survival rate for cancer of the cervix in Connecticut is due to the inclusion of many cases of carcinoma *in situ* with invasive carcinomas. Data collected in this survey do not support this hypothesis. This study reveals no explanation of why there is an appreciable difference between the incidence rates for cervical cancer or the survival rates of cervical cancer patients in Connecticut and in the Southwest Region of England. In both areas corpus cancer was more common than cervical cancer. The cervix-corpus ratio was 0.75 in Connecticut and 0.82 in the Southwest Region of England. The low ratio in England is noteworthy because cytologic methods for the detection of carcinoma *in situ* were not in general use at the time of the study.

## SUMMARY

A combined pathological and statistical survey of cancer of the uterus in Connecticut and the Southwest Region of England was undertaken to study differences between cervical cancer incidence rates and the survival of cervical cancer patients in the two areas. Diagnostic criteria for invasive uterine cancer were found to be the same in the two areas, and there were no appreciable differences in standards of reporting or registration of cases. However, carcinoma *in situ* was reported much more often in Connecticut than in the Southwest Region, primarily because of more extensive vaginal cytology programs and more liberal criteria for diagnosis.

Preliminary analysis of the data on histological features of the invasive squamous cell carcinomas in each area does not explain the observed differences in survival rates. However, the data suggest that the carcinomas in patients in the Southwest Region of England were considerably more extensive at the time of diagnosis than those in Connecticut patients.



## Criteria for Evaluating Treatment

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TO estimate the treatment results of malignant tumors it is necessary to ensure certain qualifications of the material: 1) All cases diagnosed should belong to a geographically defined area; 2) there should be uniform rules for the classification of the cases, *i.e.*, a clear anatomical definition of the tumor (for instance, the border between a carcinoma of the rectum and a carcinoma of the colon); 3) it is imperative that all cases be histologically proved; 4) the principles of treatment and those of staging should be so simple that they can easily be adopted by every physician.

The treatment results can be estimated first with regard to the histological findings. The initial histological examination of the disease may well clarify the malignancy grade of a few types of tumors (breast, rectum, uterine corpus, and ovary).

Secondly, the grade of malignancy could be estimated on surgery (or postmortem examination), which is the most exact method, provided a careful examination is carried out on the organs removed. American investigators have shown that in patients with carcinoma of the cervix, stages I and II A, there were gland metastases in 32 percent routinely examined, while after serial sections gland metastases increased to 47 percent. This classification with regard to the pathological-anatomical extension is justified, provided all patients are operated on and the surgical specimen is carefully examined. As this cannot be done in all types of tumors, it is necessary to have a clinical staging.

There are several choices available. Judging the anatomical extension of the tumor is the method usually used. This was practiced initially in carcinoma of the cervix and later in carcinoma of the corpus and vagina. At the proposal of Doctor Denoix, the International Union Against Cancer has recommended a staging with respect to (a) the tumor, (b) the glands, and (c) the metastases. With the tumor, a division according to size, extension, and fixation (T: I-T: IV) has been made. The

glands have been subdivided with regard to size and fixation (N:I-N:III), and the metastases with regard to presence (M:O-M:+). In the presentation of data on carcinoma of the cervix, it is impossible to evaluate the end results without regard taken of the staging. I would like to illustrate this with the experience of the Radiumhemmet. In 1951, Kottmeier presented an investigation, according to the Stockholm method, of the dosage distribution of radium in the pelvis of patients with carcinoma of the uterine cervix. He showed the significance of intrauterine radium in endocervical tumors, tumors with paracervical growth, and tumors with local lymph node metastases.

A few years ago an investigation was made at the Radiumhemmet on the results of treatment of 258 patients with carcinoma of the cervical stump, who had not been treated with intrauterine radium. This investigation showed that the apparent 5-year recovery rate was 62 percent. This appeared to be a surprisingly good result compared with that of the total patients with cervical cancers treated with intrauterine radium, for which the corresponding figure was 42 percent. This may prove that our evaluation of intrauterine radium was wrong. A careful analysis showed, however, that more than 50 percent of the cases of carcinoma of the cervical stump were allotted to stage I, while in the other material the corresponding figure for stage I was 17 percent. Some difference, though not so pronounced, was valid in stage II cases. It is, therefore, imperative to divide the material into four clinical stages with a clear definition of each stage to get a true picture of the treatment results.

## Clinical Trials on the Treatment of Cervical Carcinoma, Stage I

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THE clinical trials to be reported were carried out in 1957-59 at the Norwegian Radium Hospital. As a background, it is necessary to give a brief survey of the previous treatment and results.

The primary treatment of cervical carcinoma at the Norwegian Radium Hospital has always been intracavitary radium with a modified Paris method, but a relatively high number of patients, considered as good surgical risks, have had simple hysterectomy 6 to 8 weeks after radium therapy, with removal of both ovaries (Schjött-Rivers) or radical hysterectomy, with pelvic lymphadenectomy (Dahle). With both methods, promising results have been achieved. Both authors, however, admit that their patients were a select group, since only relatively young and healthy women were subjected to surgery.

The last 5-year period before the trials comprised 367 patients, 171 of whom had surgery; the operation rate was thus 47 percent. More than half of these patients had radical hysterectomies with lymphadenectomies; their 5-year survival rate was 85 percent. Those without surgery but who received X-ray treatment after radium had a 5-year survival rate of 69 percent. Of the total cases there were 83, 78, and 77 percent survivors at 3, 4, and 5 years, respectively.

During 1957-58 a series of 100 unselected patients with stage I cervical carcinoma were given betatron therapy with a 31 Mev machine, immediately following the radium treatment, which delivered to the pelvic wall a dose of 4000 r Victoreen for 3 weeks.

An increase from 42 to 110 beds in the gynecological department provided opportunity for detailed study of the localization of recurrences. This study indicated that their most frequent site was not the cervix but the parametrium and probably often the lymph nodes. Since early experiences with betatron therapy on lymph node metastases were not very promising, it was decided to try a surgical attack. Preferably this surgery should be of a type that could be applied on all patients, not only



the good operative risks. Extraperitoneal lymphadenectomy appeared to be suitable for this purpose. We had an efficient follow-up service. The cervix was easily accessible, and we believed it should be possible to diagnose a recurrence at this site relatively early. For this reason a prophylactic removal of the uterus was perhaps not strictly necessary. The diagnosis of lymph node metastases on the pelvic wall, however, was a far more difficult problem. The time when these were still amenable to treatment could easily be missed. Thus we found it clinically justified to switch from prophylactic hysterectomy to prophylactic lymphadenectomy. All patients classified as having cervical carcinoma, stage I, during 1959 were handled in the following way.

All 117 patients had primary radium treatment. In 15 there was either severe contraindication to surgery or the patients refused surgery. The rest of the patients were discharged from the hospital after radium treatment and readmitted 6 to 8 weeks later. If there were no clinical, cytological, or histological signs of residual tumor of the cervix, an extraperitoneal lymphadenectomy was performed. Then, if histological examination did not reveal lymph node metastases, no further treatment was given; if lymph node metastases were present, postoperative betatron therapy was applied. If there was suspicion of residual tumor, a radical hysterectomy with lymphadenectomy was performed. Again, in lymph node metastases, betatron therapy was given. Of the 117 patients in stage I, 102 had surgery—an operative rate of 87 percent. Twelve patients had radical hysterectomy with lymphadenectomy; 5 had total hysterectomy with lymphadenectomy; and 85, extraperitoneal lymphadenectomy.

## RESULTS

### The Radium-Betatron Series

The radium-betatron series was planned as unselected and consecutive. However, when the criteria for this were checked it was found that the series could not be defined as one sole treatment from a certain date to another. The series was tapering off to both sides, with only 53 cases left that fulfilled the criteria for a consecutive series. The curves for percent survivors, however, were practically identical, which indicated that all 100 stage I cases could be considered as unselected. The survival curves were very similar to those for the 1952-56 period.

Twenty-six recurrences or persistent lesions resulting in death were located as follows: in the cervix, 8, 3 also in the parametrium; only in the parametrium, 13; remote metastases to the lung or supraclavicular region, 2; undetermined location or death from intercurrent disease, 3.

Twelve of these patients had severe irradiating pains with swollen legs, which presented a difficult therapeutic problem, with a depressing effect on the nursing staff who had to care for them.



## The 1959 Series

The percent survivors at 3 and 4 years are 89 and 88, respectively, which indicates a striking improvement in the results. The survival rate, so far, is 89 for the patients who had surgery and 73 for those without surgery.

The incidence of lymph node metastases in the 102 surgical patients was 23 percent, and that of residual tumors diagnosed at the time of the initial treatment, 10 percent.

Among the 102 patients subjected to lymphadenectomy there were 11 deaths; 5 by progression of the local disease in spite of additional surgery and irradiation, 3 by lung metastases without pelvic recurrences, 1 by lung metastases associated with local recurrence, and 2 by intercurrent diseases without signs of local recurrence.

Only 2 of the 117 patients developed the distressful clinical picture of severe pains associated with swollen legs, compared to 12 in the 100 treated with betatron, as mentioned previously.

Table 1 shows the relation between the presence of residual tumor in the cervix after radium therapy and the presence of lymph node metastases and survival.

From these results, it may be justifiable to conclude that surgical removal of pelvic lymph nodes after radium application combined with postoperative betatron therapy of 4000 r Victoreen in the lymph node area, in positive cases, seems to have been a more effective therapy than solely this type of irradiation after radium application.

When radical hysterectomy with pelvic lymphadenectomy is reserved only for patients with clinical, cytological, or histological suspicion or proof of residual primary lesion after the radium application, and extraperitoneal pelvic lymphadenectomy for the rest of the patients, a higher percentage can have their pelvic lymph nodes removed prophylactically without undue risk.

A reliable follow-up service is necessary so that recurrences can be treated as early as possible.

TABLE 1.—Cervical cancer, stage I cases subjected to lymphadenectomy, 1959

Residual tumor after radium therapy	Lymph node metastases	Alive	Dead	Total
—	—	71	3	74
—	+	14	4	18
+	—	5	0	5
+	+	1	4	5
		91	11	102



## Results of Treatment of Adenocarcinoma of the Uterine Body

ODDMUND KOLLER, *Det Norske  
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THIS report deals with cancer of the uterine body treated at the Norwegian Radium Hospital during the years 1932-57. *In situ* lesions and sarcomas are excluded. Only histologically proved adenocarcinomas are included. The number of patients with lesions of the uterine body where the diagnosis has not been histologically confirmed is negligible.

In Norway, the treatment of cancer of the uterine body is not centralized to the same extent as cervical cancer. However, an increasing proportion has been referred to the Norwegian Radium Hospital. A maximum of 50 percent of the total number of new cases has been treated during recent years. This development is illustrated by the number of patients treated in the first 5-year period, compared to the last 5-year period: 49 and 265, respectively. The sum total of treated patients was 960.

Based on the records, all cases were classified for this report according to the international rules adopted for "Annual Reports on the Results of Treatment of Uterine Cancer." Stage I means that the cancerous process at the initial clinical examination is confined to the uterus. Stage II means that the cancer has progressed outside the uterus. The proportion of cases allotted to stage I has shown an irregular and far from statistically significant increase, from 80 percent in the first to 86 percent in the last 5-year period.

The principles of treatment have been fairly constant during the whole period. Stage I patients considered as good surgical risks have been operated on primarily and received postoperative radiation. In less favorable operative risks, radium packing has been given a trial and, if unsuccessful, the patients have been operated on. In poor operative risks the therapy has been by irradiation alone. Stage II patients have also been treated solely by irradiation.

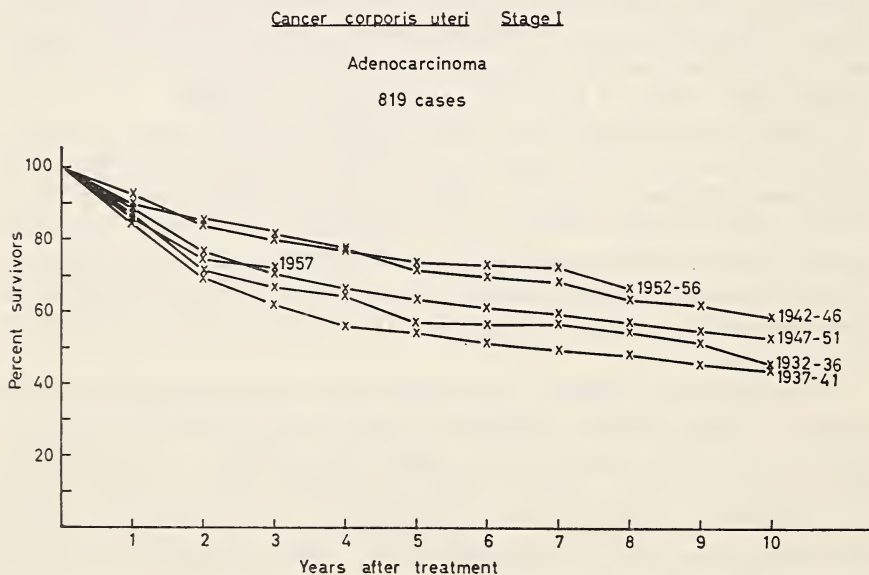
## RESULTS

The results obtained in stage I and stage II cases were markedly different. The 5-year survival rates were 67.5 and 23.6 percent, respectively.

In stage I, operated patients had a better prognosis than patients treated only by radiation. The 5-year survival rates for the three treatment groups were:

Surgery + postoperative radiation	75.5%
Surgery + preoperative radiation	67.8%
Radiation only	42.6%

Patients treated by surgery plus postoperative radiation in recent years (1952-57) had a somewhat higher survival rate than in earlier years, but the difference is not statistically significant. There was no significant change over time in the survival rates for patients who received preoperative radiation. Patients treated by radiation alone in the more recent period (1952-57) had a lower survival rate than in earlier years. The combined effect of these changes in survival for stage I patients treated by different methods is shown in text-figure 1. The curves indicate an increased survival rate in the 1952-56 period compared to earlier periods, but the difference does not appear to be statistically significant. The increased survival rate in the 1952-57 period may be accounted for by the increased proportion of patients subjected to primary operation, whose survival rate has probably increased. The increased proportion of primary operations and the increased survival rate in these patients seem to



TEXT-FIGURE 1.—Survival curves for patients treated in successive calendar periods.



have more than eliminated the opposing effect of the decreased survival rate in the other treatment groups. The decreased survival rate in these treatment groups may have been caused by selection. Changing criteria for the selection of patients for preoperative radiation and for radiation therapy is suggested by the fact that patients in these two treatment groups were older in the more recent period.

Available data on stage II patients indicate no change over time in survival.

It may be concluded then that, during a period in which principles of treatment of endometrial adenocarcinoma have remained practically unchanged, the survival rate in stage I cases nevertheless seems to have been increased. This may be accounted for by the significant increase of the proportion of patients who have been subjected to primary surgery and the probably increased survival rate following this treatment.

In the patients subjected to preoperative radiation or treated solely by irradiation, survival rates tend to be reduced. This may be accounted for by the increasing trend in recent years to reserve this type of treatment for older patients.

The Norwegian Radium Hospital treats only about 50 percent of the total number of endometrial carcinomas in Norway. The present material, therefore, is a selected one and may reflect a tendency among the Norwegian doctors to refer the cases with the poorest prognosis to the specially equipped cancer hospital.

## Summary of General Discussion

### Cervix

The discussion was mainly an effort to explain the observed differences in survival rates between England and the other countries covered by the report. The fact that the incidence of carcinoma of the cervix is related to social status and sexual behavior raises the question whether these factors also influence the survival rates. Different types of disease may occur in geographic areas with different social conditions. More studies of this important issue are clearly needed. Three studies from the United States were quoted, which did not show any difference in survival among the different income groups or between the urban and rural population. However, there may be greater differences in social and environmental factors among the socioeconomic groups in Europe than in the United States.

Both the attitude of women concerning genital tract symptoms and the attitude of the medical profession may affect the frequency with which early lesions are diagnosed. It was pointed out that British women in the premenopausal group may be somewhat more negligent concerning the presenting symptoms of cancer than those in the postmenopausal group. However, this argument is partly contradicted by the fact that survival rates for cervical cancer in England and Wales were relatively low in all age groups.

Delay in diagnosis may not affect the distribution of cases with respect to stage, but may result in larger tumors and in more glandular involvement within each stage group. This might depress the survival rates for each stage.

In the discussion of the need for earlier diagnosis, the importance of cytologic screening programs was emphasized. The optimal value of cytologic screening can be obtained by careful selection of high-risk groups. As an alternative to the somewhat laborious cytologic screening, a method for detection of cancerous tissue by enzyme analysis is presently being tested in London.

It was shown that the ratio of cervix to corpus cancer in Connecticut started to decline before the cytologic screening programs were initiated and that a similar decrease had been noted in countries both with and without such programs. Denmark, with the highest survival rates reported for cervical cancer, did not have a cytologic screening program during the calendar period covered by the data presented. These observations suggest that the incidence rates of cervix cancer may be influenced by factors other than early diagnosis and the detection of precancerous lesions—factors about which we know nothing.

It was recognized that the analysis of mass data cannot provide as definitive a conclusion concerning the relative merits of different treatment methods as can be obtained from controlled clinical trials. The available data suggest that it may be useful to test via clinical trial the relative value of primary surgery, primary radiation, and combined therapy in treating early cancer of the cervix.

### Corpus

The report on corpus cancer showed considerably lower age-adjusted survival rates for Finland and Norway than for the other countries covered. The discussion revealed that these variations might be due to differences in data collection and handling at the various registers. It was pointed out that Finland and Norway have a very good checkup system on cases first reported by death certificates, which thus brings the "Death Certificate Only" group down to a minimum. This group of patients, excluded from the tabulated data, comprises 9 percent of the Connecticut material compared to 0.7 percent in the Norwegian material. This makes the number of untreated patients in Norway apparently high in comparison. A revision of the data adjusted for this difference in registry practice yields end results for Norway and Connecticut differing only by 2 to 3 percent. The same holds true for the Finnish data.

The need for more detailed analysis of the data presented was stressed. From the public health point of view, it is interesting to determine the survival of the total group of patients, regardless of therapy. Clinicians, on the other hand, want to know the results for treated patients. A relevant question in a comparison of results in different countries is: What proportion of patients were treated in hospitals?

The number of women within each age group of the total population who have had hysterectomies is an important fact to be investigated in interpreting the incidence of cancers of the corpus.

Another subject suggested for further study was the variation in the survival curves after the 5th year following treatment. For example, the Connecticut curve is flat, while the Danish curve drops.





## **Cancer of the Breast**

Breast Cancer—Evaluation of End Results. J. LEGUERINAIIS and XAVIER GELLÉ, France

Adjuncts to the Treatment of Breast Cancer. J. L. HAYWARD, England

Results of Simplified Treatment of Breast Cancer. GEORGE CRILE, JR., USA

A Clinical Trial in Cancer of the Breast. S. KAAE, Denmark

Results of Early Detection of Breast Cancer. VICTOR A. GILBERTSEN and OWEN H. WANGENSTEEN, USA

### **GENERAL DISCUSSION**

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Presented at the International Symposium on End Results of Cancer Therapy,  
Sandefjord, Norway, September 16-20, 1963.



## Breast Cancer—Evaluation of End Results

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*Paris, France*

A few years ago the Ad Hoc Group on International Cooperation in Evaluation of End Results was established under the sponsorship of the National Cancer Institute, Bethesda, Maryland, USA. Data were received from cancer registries in Denmark, England and Wales, Finland, France, Norway, and the United States. The data were distributed among the various agencies entrusted with the analysis of information about a given site of cancer.

The homogeneity is not perfect among these registries. Some cover exhaustively all the cases of the country, as in Scandinavia; others register only part of the cases or even sometimes a biased selection, as in France, where the patients are only those seen in Cancer Centers. Comparisons between these registries, therefore, have only a relative significance but are nonetheless interesting.

In 1962 France was assigned the study of breast cancer, and, except for Denmark, all other registries sent in their data. These data and those of the French Permanent Cancer Survey are the basis of this study.

This report is restricted to primary malignant tumors of the breast observed among women in the following age groups: 0-44, 45-54, 55-64, 65-98, and all ages together. As we deal only with women, there will be no study of sex ratio, and no comparison of end results for the 2 sexes; and since only histologically confirmed cases are taken into account, there will be no comparison between confirmed and not confirmed cases. The total of cases was 68,000, but some considerations led us to discard 23,000 diagnosed prior to 1950, and we will actually deal with some 45,000 cases.

Because of differences in classifying stage of disease in the various countries the cases were divided into two main groups:

*Group I*, "localized" (about 40% of the total): small- or medium-sized tumors, not adherent to pectoralis major muscle, without lymph node involvement, and without metastasis.

*Group II*, "invasive": all other cases. This rather elementary division allows a reasonably satisfactory partition of the cases.

Five methods of treatment have been distinguished: 1) surgery; 2) X-ray therapy; 3) X-ray therapy plus surgery; 4) other treatments (chemotherapy, hormones); 5) untreated cases (which for breast cancer are very few).

The results were studied on the basis of survival rates corrected for life expectancy by means of actuarial methods involving the use of an electronic computer. The results shown in the tables are accordingly given in the corrected survival rates (C.R.) and are difficult to compare with the crude survival rates or apparent recovery rates of similar studies on various malignant tumors.

### SELECTION OF THERAPEUTICAL METHODS

Every country has its own therapeutical trends (table 1). In the "localized" group corresponding to what could be called the "good cases," surgery is used more in the United States. A different trend is noted in European countries: Norway has a preference for radio-surgical combinations. This is noted, too, but in a lesser form, in England and Finland. France alone shows an almost equal distribution among the three major methods of treatment. In tumors of Group II, the same tendencies are

TABLE 1.—Percentage distribution of treatments

		Group I (localized)—all ages		
		Surgery	Radiation	Surgery plus radiation
Europe	{ France	0. 30	0. 22	0. 44
	{ England and Wales	0. 28	—	0. 60
	{ Finland	0. 18	—	0. 75
	{ Norway	0. 10	—	0. 90
United States	{ Connecticut	0. 86	—	0. 08
	{ U.S. Hospitals	0. 78	—	0. 17
	{ U.S. Central	0. 90	—	0. 08
		Group II (not localized)—all ages		
		Surgery	Radiation	Surgery plus radiation
Europe	{ France	0. 10	0. 33	0. 51
	{ England and Wales	0. 20	0. 09	0. 70
	{ Finland	0. 18	—	0. 80
	{ Norway	0. 06	0. 05	0. 85
United States	{ Connecticut	0. 65	—	0. 28
	{ U.S. Hospitals	0. 54	0. 09	0. 34
	{ U.S. Central	0. 64	0. 06	0. 25



noted, though with a little less surgery alone and a little more surgery plus X ray. Therapists, in spite of their personal inclinations, admit the complementary safety of postoperative X-ray therapy where lymph nodes are involved. These therapeutic trends are independent of the age of patients.

The reasons for these important differences in therapeutic practice are difficult to explain. It is hard to believe that the treated patients are so different. Their distribution into two main groups (I and II) is easy and involves no subtlety in interpretation. The percentage of patients of Group I is uniform in the various countries (about 42%) and the age groups in the different registries are remarkably alike.

Thus, since there is a similarity in the human material, why are there such different therapeutic methods? In France, the heads of the Cancer Centers are mostly radiologists, which partly explains why 60 to 75 percent of the patients are treated by radiation. It would be interesting to know why this method of treatment is so rarely used in the United States.

## RESULTS ACCORDING TO TREATMENT

This study is difficult because we cannot compare the results of one type of treatment in two countries, when one rarely uses it while the other uses it in 80 or 90 percent of the cases. But we can compare the same treatment in the registries where it is used with a similar frequency, *e.g.*, surgery between 2 of the 3 U.S. registries, or combination surgery plus radiation in Europe. We can also compare 2 different treatments within the same country, if they are both frequently used, *e.g.*, surgery and surgery plus radiation in France for Group I and in the United States for Group II, and 2 different treatments in 2 countries, *e.g.*, surgery plus X rays in France and Norway with surgery alone in the United States.

As a general rule, the results of surgery alone are better than those of X ray and surgery combined (table 2), primarily because the surgeon passes on to the radiotherapist the patients he worries about, that is, those with rather poor prognoses.

TABLE 2.—Corrected survival rates at 5 years, according to treatment—all ages

	Treatment	U.S. Central	England and Wales	France
Group I (localized)	Surgery	0. 85	0. 80	0. 86
	Surgery plus radiation	0. 76	0. 70	0. 72
Group II (not localized)	Surgery	0. 50	0. 50	0. 53
	Surgery plus radiation	0. 44	0. 47	0. 46

TABLE 3.—Corrected survival rates at 5 years in different registries—all ages, all treatments

	U.S. Central	U.S. Hospitals	Connec- ticut	Nor- way	England and Wales	Finland	France
Group I (localized)	0. 83	0. 82	0. 79	0. 81	0. 73	0. 72	0. 74
Group II (not local- ized)	0. 44	0. 40	0. 42	0. 42	0. 44	0. 39	0. 39

## RESULTS ACCORDING TO COUNTRY

Comparisons between countries (or registries) are not free from criticism. These registries have neither the same basis nor the same scope; some record all the cases, others only a portion of them. However, the similarities we noted before allow us to make some observations.

If we add the figures for all ages and treatments, the results are better for Group I (localized) in the United States and Norway than for the three other European registries (table 3). The C.R. for the 5-year survival averages 0.81 against 0.73. For Group II, differences are not significant, ranging from 0.39 to 0.44.

It is to be noted (table 1) that Norway nearly always uses the combination surgery plus radiation while in the United States surgery alone is applied to about 80 percent of the patients; very different treatments yield similar results. It is an interesting observation that ought to settle doctrinal disputes on the "best" methods of treatment.

## RESULTS ACCORDING TO AGE

Emphasis has often been placed on the bad prognosis of breast tumors occurring before the menopause in contrast with a more favorable outcome in older women. Table 4 shows that this is not confirmed within the same country (or registry). In France and England the 5-year survival rates in the older women are a little better than those observed in younger women. In other countries (Norway, U.S. Central) the reverse is observed, but at any rate the variation is small and without great significance.

TABLE 4.—Corrected survival rates at 5 years according to age group; all treatments—Group I (localized)

Age group	U.S. Central	Connecticut	Norway	England and Wales	Finland	France
0-44	0. 83	0. 81	0. 84	0. 71	0. 78	0. 71
45-54	0. 81	0. 80	0. 81	0. 74	0. 72	0. 75
55-64	0. 83	0. 79	0. 82	0. 74	0. 68	0. 74
65-98	0. 84	0. 78	0. 78	0. 75	0. 71	0. 77

Thus within a country the age influence on the prognosis of breast cancer is negligible. Such a conclusion is possible only through use of corrected survival rates for life expectancy.

### CONCLUSIONS

Among the member countries of our Ad Hoc Group there is some homogeneity in the end results for breast cancer. In the prognosis (*a*) the *stage* of the *tumor* is a main factor. Group I (localized) gives a C.R. of about 0.80 for 5-year survival rate. Group II (invasive) does not exceed 0.40 and, unfortunately, it is the most frequent. (*b*) The *method of treatment* is less important than it might be thought (*cf.* table 2). (*c*) Contrary to previously held opinion, the age of the patient seems to make little difference in the prognosis.

Only international cooperation, involving scores of thousands of cases, has made possible these comparisons between various countries. From them, conclusions based on clinical and statistical grounds can be drawn. All credit for this must go to our Ad Hoc Group.





## Adjuncts to the Treatment of Breast Cancer

J. L. HAYWARD, MB., F.R.C.S.,<sup>1</sup> *Imperial Cancer Research Fund and Guy's Hospital, London, England*

### EARLY BREAST CANCER

SINCE radical mastectomy was introduced in 1894 by Halsted and Meyer (1, 2), it has generally been considered the standard treatment for early cancer of the breast. Various attempts to introduce lesser techniques, such as simple mastectomy followed by radiotherapy as advocated by McWhirter (3), have not met with general approval. Similarly, more extensive procedures involving continuity resection of the internal mammary chain (4), although possibly of use for medial half growths, have not been widely adopted. Unfortunately neither these nor any other alternative to the radical operation has been subject to controlled clinical trials and, therefore, no valid comparisons can be made. It is generally accepted, however, that with radical mastectomy as the primary treatment of localized operable cancer of the breast, a 5-year survival rate of approximately 60 percent can be achieved.

In an attempt to improve this survival rate and decrease the incidence of recurrences, various adjuncts to radical mastectomy have been introduced over the years. Those most commonly employed include postoperative radiotherapy, oophorectomy or ovarian irradiation, and synoperative chemotherapy. Recently these treatments have been the subject of controlled clinical trials and consequently their value can be critically assessed.

#### Postoperative Radiotherapy

Postoperative radiotherapy is so widely used following radical mastectomy that it is generally regarded as a part of the primary treatment. It

<sup>1</sup> The trials comparing early and late endocrine ablation and the results of cortisone therapy are being undertaken in cooperation with Professor Hedley Atkins and Dr. Kenneth MacLean of Guy's Hospital, London, and Mr. Murray Falconer and Mr. Peter Schurr of the Guy's Maudsley Neurosurgical Unit, London.

TABLE 1.—Percentage mortality at 5 and 7 years of patients subjected to postoperative radiotherapy (5)

Years	Quadrate		Peripheral	
	Percentage mortality		Percentage mortality	
	Treated	Watched	Treated	Watched
5	45.0	43.5	43.5	39.0
7	54.6	52.0	51.0	49.0

is considered particularly valuable when the axillary lymph nodes are involved with metastatic carcinoma. Although techniques vary throughout the world, most commonly the axillary, supraclavicular, and internal mammary fields are treated.

Recently Cole (5) described the results of a trial previously reported by Paterson and Russell (6) in which the crude mortality rate of a group of patients treated postoperatively by radiotherapy was compared with that of a control group treated only if or when metastases subsequently occurred. The patients were allotted to the two groups by random sample and over 700 were included in each group. Table 1 shows the mortality rates in the trial expressed as a percentage at 5 and 7 years. Two techniques were used, a quadrate and a peripheral, but with neither method did the difference in mortality rate achieve statistical significance.

### Ovarian Irradiation or Oophorectomy

Most workers agree that castration by radiation or surgical operation achieves the same result. The case for and against prophylactic castration in early breast cancer has been argued for many years, and recently the literature has been extensively reviewed by Lewison (7) who concluded that following this treatment there is a well-defined trend toward a prolonged life expectancy and an improved survival rate. However, the only clinical trial involving random selection is that reported by Cole in 1962 (8). Here, 293 patients who were given postoperative ovarian irradiation were compared with 305 controls. All the patients were premenopausal or within 2 years of the menopause, and the two groups

TABLE 2.—Percentage survival of patients subjected to ovarian irradiation after mastectomy, compared with controls (8)

Number of patients		Percentage survival at 5 years	
Radiated	Control	Radiated	Control
293	305	65.5	58.4

TABLE 3.—Percentage recurrence at 5 years following ovarian irradiation (8)

	Percentage at 5 years		Statistical significance
	Radiated	Control	
Recurrence in original breast area	20. 8	27. 2	$P = 0. 07$
New growth or recurrence, other breast areas	7. 8	11. 5	$P = 0. 14$
Metastases: Bone, liver, lung, and brain	31. 4	40. 0	$P = 0. 03$

were chosen by random sample. Table 2 shows that there was an increase in the survival rate at 5 years for the group subjected to ovarian irradiation. This difference between the two groups, however, did not achieve formal significance.

There was a more marked difference when the incidence of distant metastases was considered and here the percentage incidence at 5 years for the irradiation group was significantly less than that of the controls (table 3).

### Synoperative Chemotherapy

This treatment involves the prescription of a cytotoxin at the time of operation so that the patient has a chemotherapeutic cover when considered at the greatest risk from blood-borne tumor emboli. In 1961 the Surgical Adjuvant Chemotherapy Breast Group reported the progress of a trial carried out to determine the efficiency of synoperative cytotoxins in the treatment of breast cancer (9). In a strictly controlled experiment a group treated by radical mastectomy plus tris(1-aziridiny)phosphine sulfide (thio-tepa) is being compared with a group treated by radical mastectomy alone. Preliminary results indicate a statistically significant decrease in the number of early recurrences among patients who received thio-tepa as adjuvant therapy. No difference in survival rate has yet been shown, and the trial is being continued.

### New Methods

It has recently been reported that many patients with early breast cancer excrete subnormal amounts of androgen metabolites and possibly greater than normal amounts of corticosteroids (10). It has also been shown that these patients with an abnormal steroid excretion have a bad prognosis following mastectomy (11). A trial is now being started in which patients after mastectomy are being treated for a long period with small doses of androgens. These patients will be compared with controls selected by random sample who will receive no such treatment. No results of this trial are as yet available.



## ADVANCED BREAST CANCER

There are many treatments that influence the course of advanced breast cancer. The value and indications for most of these are known, but in no case is the true method of action appreciated. Similarly, although there is no doubt that the quality of life can be improved in certain cases, there is little direct evidence of alteration in the survival rate.

### Oophorectomy or Ovarian Irradiation

This was the first method used to influence the hormone environment in advanced cancer of the breast. Beatson in 1896 first described the benefit which could follow surgical removal of the ovaries (12), and in 1922 De Courmelles showed that a similar effect could be obtained from ovarian irradiation (13). It is generally accepted that 20 to 25 percent of patients so treated will improve and that this improvement may last up to 3 or 4 years. Lewison (7) in his review states that, in those patients showing an objective improvement, there is an associated increase in survival time. Although this result has been inferred in many reports, there is no confirmation from a properly controlled clinical trial. Cole (8) did, however, compare a group of 76 women with advanced or recurrent cancer, who had ovarian irradiation, with 73 controls. Both groups were selected by random sample. No significant difference was noted between the survival rates of the two groups. In the irradiated group 30.3 percent of patients survived for 5 years, whereas in the control group 28.8 percent survived to that time.

### Androgens

Androgens, first introduced in 1942 by Farrow and Woodard (14), are still prescribed extensively for the premenopausal patient. The disadvantages of virilization encountered with the early androgens have now largely been overcome with modern synthetic drugs. A remission rate of about 20 percent can be expected, similar to that obtained from ovarian extirpation. Possibly the two methods of treatment may act in the same way. The remission in favorable cases can last 3 to 4 years.

No controlled clinical trial has been carried out comparing treated with nontreated patients, and although the quality of life can be improved there is no direct evidence of any effect on survival rate.

### Estrogens

Although the retarding action of certain polycyclic hydrocarbons on animal tumors had been known for some time (15), it was not until 1944 that the first series was reported of 73 patients with breast cancer treated with synthetic estrogens (16). Diethylstilbestrol is now used extensively



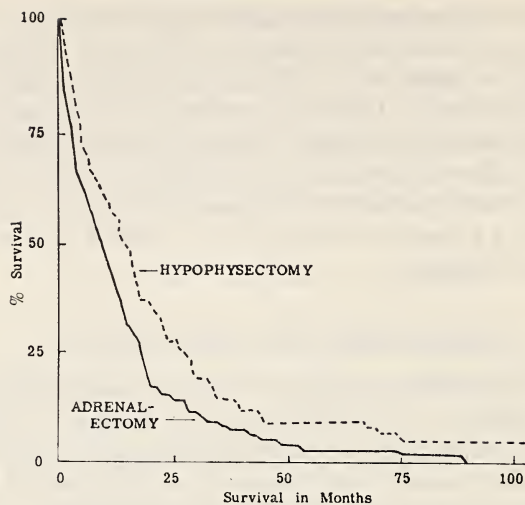
in the treatment of advanced breast cancer in postmenopausal patients and is successful in approximately 40 percent of the cases. There is good evidence that both the expectancy (17) and the quality of survival (18) are greatest in old patients. Indeed, in patients over 70, remission can be expected in 60 percent of the cases. Perhaps because of the simplicity of prescription and the relative lack of side effects, no trial has been carried out comparing treated patients with untreated controls. No information is available on any increase in survival rate as a result of treatment, though this is frequently inferred.

### Adrenalectomy and Hypophysectomy

The general availability of cortisone for oral administration made removal of the adrenal and pituitary glands feasible. Following their introduction in 1952 and 1953 (19, 20), adrenalectomy and hypophysectomy became widely used in the treatment of disseminated cancer of the breast. It is now generally recognized that a remission rate of approximately 40 percent can be expected with an operative mortality of between 5 and 10 percent. In exceptional cases, benefit can last up until about 8 years but in no case has a cure been reported. No series has been published in which patients subjected to hypophysectomy or adrenalectomy have been compared with controls who have not had the operations. A trial has, however, been carried out in which a group of 79 adrenalectomized patients was compared with a group of 70 subjected to hypophysectomy (21). All these patients had had previous hormone therapy and were selected by random sample. The study showed a significantly greater degree of benefit in the hypophysectomized group as measured by the "Mean Clinical Value." A life table constructed from the results is shown in text-figure 1. The difference in proportions surviving at 3 months is significant ( $0.04 < P < 0.05$ ), but the difference in the expectation of life—14.2 months for adrenalectomy and 20.3 months for hypophysectomy—although apparently considerable is not statistically significant.

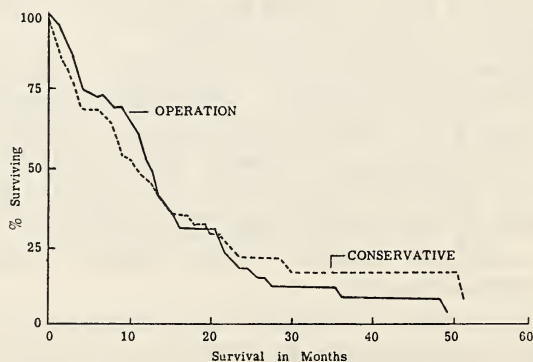
As previously mentioned, this trial was carried out only on patients who had had previous hormone therapy. This hormone therapy had been applied for at least 4 to 6 weeks before a decision was made whether or not the patient was improving. Inevitably, because of this, some patients became too ill for subsequent operation or died before further treatment could be applied. It was thought that, if adrenalectomy or hypophysectomy was carried out without previous hormone therapy, a better survival rate might be observed.

Three years ago a trial was begun to compare the survival of patients who were treated immediately by hypophysectomy or adrenalectomy and without previous hormone therapy (operation group), with those who were treated with hormones first (conservative group). Operation was only offered to the second group if or when hormone treatment failed.



TEXT-FIGURE 1.—Life table comparing the survival rates following adrenalectomy and hypophysectomy.

The patients were allotted to each group by random sample, and so far 134 patients have been admitted to the trial—67 in each group. Text-figure 2 illustrates a life table constructed to show the proportional survival to date in each group. The expectation of life on the two sides of the experiment is almost identical—15.8 months for the operation group and 16.7 months for the conservative group. The premise on which the experiment was based was confirmed; of the 67 patients in the conservative group 25 or 37 percent died while on hormone therapy or deteriorated to such an extent to prohibit a subsequent operation being carried out. This



TEXT-FIGURE 2.—Life table comparing the survival rates of patients having immediate adrenalectomy or hypophysectomy (operation) with those having the operations after previous hormone therapy (conservative).

trial is still being continued and the long-term results cannot yet be assessed.

### Cortisone and Ovarian Irradiation

Ever since adrenalectomy and hypophysectomy were introduced, it has been felt that much, if not all, the benefit might be due to the cortisone administered as replacement therapy, rather than to the operation. That cortisone therapy and ovarian extirpation could indeed cause some cases to regress was shown by Nissen-Meyer in 1955 (22), but the question as to whether this was a substitute for adrenalectomy or hypophysectomy has not yet been answered. Dao, Tan, and Brooks (23) compared 20 patients treated with cortisone with 19 treated by adrenalectomy, the groups chosen by random sample. They found that none of the patients treated with cortisone showed a favorable objective response, whereas 44.5 percent of the adrenalectomized patients were objectively benefited. Of 7 patients who previously failed to respond to cortisone, 2 subsequently responded to adrenalectomy. In this trial, however, neither the cortisone-treated patients nor those receiving adrenalectomy had an oophorectomy or ovarian irradiation. In addition the patients were selected in such a way that all were at least 1 year post menopausal. The results were not statistically analyzed and the survival rates have not yet been compared.

A controlled trial was started 2 years ago at Guy's Hospital in which those patients who had had previous hormone therapy, and for whom normally adrenalectomy or hypophysectomy would have been prescribed, were allotted by random sample into two groups. In the first group the patients were prescribed cortisone, 75 mg daily, and received ovarian ablation by radiotherapy. If or when this treatment failed, then adrenalectomy or hypophysectomy was carried out. Patients in the second group were operated on without prior cortisone therapy, and the two groups are being compared by their response to the two procedures and by the subsequent survival rate. Forty-eight patients have so far been admitted to the trial, but no results are yet available.

## DISCUSSION

### Early Breast Cancer

The aims of adjunctive treatment in early breast cancer are twofold: 1) to affect favorably the appearance of secondaries and 2) to increase the survival rate. Radiotherapy is usually considered an essential part of the primary treatment of breast cancer but it is important to appreciate that in a series of over 1,400 patients no significant benefit could be demonstrated in a group that had received radiotherapy after mastectomy. Although local secondaries appeared more frequently in patients that were not irradiated postoperatively, these were easily treated when they



occurred and did not affect the survival rate. Indeed it seemed that by a delay of radiotherapy in this way much unnecessary treatment could be avoided at the time of operation.

Neither ovarian irradiation after mastectomy nor synoperative chemotherapy has yet been shown to improve significantly the survival rate. It would seem, however, that the apparent delay in appearance of metastases following both treatments would warrant their serious consideration. Not every clinician would recommend the haphazard castration of all premenopausal women because of a 9 percent difference in the rate of appearance of distant metastases; nevertheless the difference is there and should be taken into account.

Reports of synoperative chemotherapy are incomplete and further work needs to be done. Particularly, information is needed on the drug of choice and optimum dosage; certainly it appears as if the development of metastases can be delayed, but no information is available yet on any effect on survival rate.

### Advanced Breast Cancer

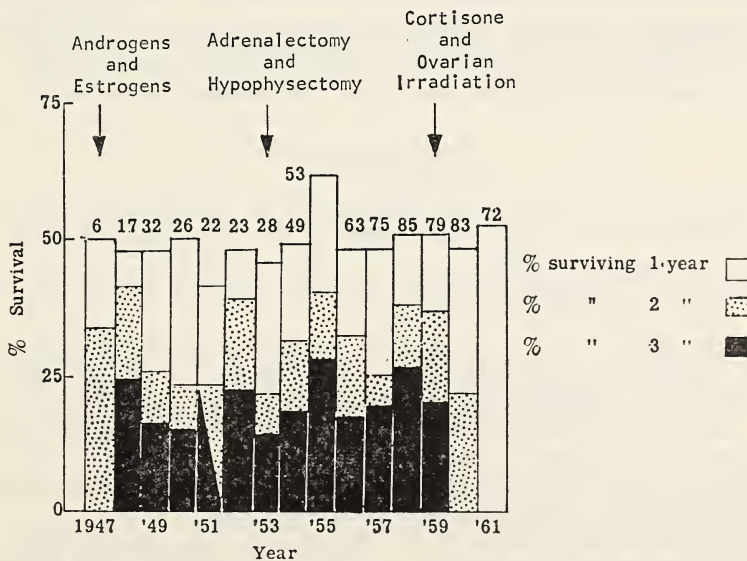
In the treatment of advanced cancer the survival rate is probably less important than quality of survival. That quality can be affected is undoubted, and frequently by simple treatments without serious side effects. If major operative treatment is considered, then the benefit to be accrued must be worth while and the chances of success as high as possible. Certainly if adrenalectomy and hypophysectomy are to be considered, then accurate selection of patients is essential. Many methods to this end have been described (24-26), but none has yet been confirmed. It is to be hoped that by one of these means it may soon be possible to exclude most of those patients who at present derive no benefit from these major procedures. There is little doubt that, when successful, hypophysectomy or adrenalectomy can give a longer period of remission than any other therapy for advanced cancer of the breast.

Whether the operations should be considered before or after the prescription of hormones remains to be seen. There are probably many factors at play and it is interesting that the curves shown in the life table in text-figure 2 cross at about the 15th month. Probably this reflects the higher proportion of the operation group surviving the first few months and may be due to the greater degree of care these women receive because of hospital admission. Those patients for whom hormones are prescribed are treated at home where conditions may not be ideal and naturally they do not receive the same degree of nursing care as the operation group. It would probably be wiser for all patients with advanced cancer to be admitted to a hospital immediately, no matter what treatment is to be applied, if the best results are to be achieved. The merits of out-patient hormone treatment may not necessarily be to the patient's benefit.



The advantages and disadvantages of various treatments for advanced cancer of the breast will continue to be debated for some time. Each method when introduced was claimed as an advance and each was superseded by therapy apparently giving greater benefit. One would therefore expect the results of treatment in advanced cancer of the breast to show an improvement over the years and an increase in the survival rate to reflect the introduction of each new treatment. Text-figure 3 shows the survival percentages of patients with advanced breast cancer seen at the Breast Clinic, Guy's Hospital, between the years 1947-61. No demonstrable difference in survival rate at 1, 2, or 3 years has occurred as a result of the introduction of new treatments. It is possible that the material referred to the Clinic varied or that the patients were more advanced in later years, but these effects are unlikely to be great. It seems rather to indicate the extremely small over-all effect produced by the so-called advances in the management of late breast cancer.

It is not to be presumed that this description of adjuncts to the treatment of early and late breast cancer is in any way inclusive, but many of these treatments are practiced assiduously today under the impression that the results of the primary therapy will be enhanced, and it is perhaps interesting to consider the evidence on this point. That the quality of life can be improved seems definite but only once was there statistical evidence of any increase in the time of survival due to treatment. This one instance—when a greater number of hypophysectomized patients were shown to be living at 3 months compared with adrenalectomized patients—



TEXT-FIGURE 3.—Survival rates at 1, 2, and 3 years of all patients with advanced breast cancer attending the Breast Clinic, Guy's Hospital, from 1947 to 1961.

could as easily have been due to adrenalectomy decreasing the survival rate as to hypophysectomy increasing it. Indeed this is partly borne out by the operative mortality in the series, which was 9 percent for adrenalectomized patients but only 4 percent for hypophysectomized patients.

This does not mean that none of these treatments can influence survival rate, but rather that this influence has not been great enough to achieve technical statistical significance in the trials so far carried out. Statistical significance is not necessarily important in itself, but the fact that some of these trials of accepted treatments have included over 1,400 patients gives some suggestion that, even if survival is affected, it is not to any great degree.

Evidence has been put forward in the past that survival is unaffected by any form of treatment, including mastectomy (27, 28). These reports received little sympathy, and new data, based on a large series of untreated patients, have since inferred the opposite (29). Such statements are confusing and most observers would agree that treatment should still be planned on the assumption that the survival rate can be affected. But in a similar fashion it would be wrong to magnify without justification the effect on end results of any particular therapy, whether primary or adjuvant.

### SUMMARY

An account is given of the various adjuncts commonly used to treat early cancer of the breast. Mention is made in each case of the effect on survival time and the subsequent development of metastases. In addition, the treatments considered of value in advanced cancer of the breast are outlined, together with an appreciation of their effect on end results. Preliminary data are also given on comparative trials now in progress.

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## Results of Simplified Treatment of Breast Cancer

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**I**MRESSED by the morbidity induced by combinations of radical mastectomy and radiation therapy, in 1955 I initiated a clinical study to see if the treatment of breast cancer could be simplified without detracting from the chances of cure. My colleagues at the Cleveland Clinic continued to use conventional radical mastectomies or modifications of the radical technique often accompanied by prophylactic radiation, while I performed mainly simple mastectomy and rarely used radiation unless there was clinical evidence of involvement of the axillary lymph nodes. There were approximately an equal number of patients in each of the groups, and no selection was employed in the assignment of the patients to one group or the other. The following conclusions were drawn from the study.

1) Of 183 consecutive patients with cancer of the breast, 75 percent were operable. Half of the operable patients were treated by radical or modified mastectomy, and half by simple mastectomy usually without radiation therapy.

2) After simple mastectomy (usually without irradiation), the 5-year and 6-year survival rates and the 5- and 6-year survival rates of patients free from disease were a little higher than similar rates after radical mastectomy with or without radiation.

3) The survival rate of patients of the surgeon who did chiefly simple operations was higher than that of patients of surgeons who did chiefly radical operations.

4) In the period in which the highest proportion of simple operations was done, the survival rate was higher than that in the period in which fewer simple operations were done.

5) The incidence of local recurrences was a little higher after radical operations than after simple ones.

6) There was no tendency in the 5th or 6th year of the study for the patients treated by simple mastectomy to show a higher rate of recurrence than did those treated by radical mastectomy.

7) Although simple mastectomy was followed by a slightly higher survival rate than was radical mastectomy, some of this difference can be explained on the basis of selection of patients.

8) Throughout the study, survival depended more on the stage of the disease in the patients selected for a type of treatment than it did on the type of treatment given.

9) In clinical stage I breast cancer, when no axillary nodes were palpable before operation, the results were a little better after simple than after radical mastectomy.

10) In clinical stage I cancer, 32.5 percent of the patients treated by radical mastectomy were found by the pathologist to have nodes involved. In clinical stage I cancer, 30 percent of the patients treated by simple mastectomy without radiation later were found to have cancer in the nodes. This was treated in most cases by axillary dissection performed from 1 month to 6 years (average, 22 months) after the mastectomy.

11) Judged by the numbers of nodes involved at the time of axillary dissection in each of the two series, there appeared to be no tendency for the cancer to spread from node to node after the primary tumor was removed. Both the absolute 5-year survival rate and the 5-year survival rate of patients free from disease were higher in patients treated by simple mastectomy and delayed axillary dissection than in those treated initially by radical mastectomy.

12) The possibility is suggested that, in occasional stage I breast cancers, prophylactic removal or irradiation of uninvolved axillary nodes may reduce the immunologic resistance of the host and favor the development of metastases.

13) Since the morbidity involved in radical mastectomy is considerably greater than that after simple mastectomy, and since prophylactic radiation also appears to increase morbidity without increasing the rate of cure, it is urged that randomized clinical experiments be planned to determine the minimum effective treatment of breast cancer.

## A Clinical Trial in Cancer of the Breast

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I agree with the former speakers that the only way to compare the different policies in the treatment of carcinoma of the breast is by clinical trials.

At the Radium Center in Copenhagen, we started a randomized study in 1951. For one group the therapeutic principle in operable cases was simple mastectomy plus postoperative irradiation by the McWhirter method. For the other group it was extended radical mastectomy by the method of Dahl-Iversen, without any supplementary irradiation. We had about 340 patients in each group.

There was no difference in total survival and in recurrence-free survival for the first 7 years after treatment, either in the total groups or in the different stages of the disease. The 5-year survival rate in clinically operable cases was 64 percent in each group. The frequency of local and regional recurrence was the same in the two groups.

It is surprising that in patients with cancer of the breast there is so small a difference in the survival rates after very different treatment policies. In this connection the investigation made by Professor Kreyberg several years ago is of interest. He indicated that a fraction of breast tumors grow slowly, without metastases, for many years. These can be cured by many methods. Another fraction is made up of very malignant tumors, with early distant metastases. These cannot be cured by any method. Between these groups are the cases of breast tumors with an intermediate growth rate and tendency to metastasize. It is only in these that the difference in survival can be expected after various treatment methods. Kreyberg estimated this last group to be a third of all breast cancer patients. If that is correct, only minor differences in survival can be expected following the various treatment methods.

May I point out another problem. Haagensen, at the Columbia Medical Center in New York, has the best results of all after treating carcinoma of the breast, in operable cases, by radical mastectomy. This is partly due to

a high grade of selection. He starts the operation with triple biopsies from the top of the axilla, the supraclavicular region, and the internal mammary chain. Patients with any of those areas showing, by frozen sections, metastases are referred for irradiation without further surgery, or, at most, simple mastectomy is done. Dr. Guttmann at the Delafield Hospital in New York, treating these referred cases by supervoltage irradiation, has 5-year recurrence-free survival of about 50 percent. This may indicate that surgery is the best method for early breast cancer and that irradiation is better for regional, more advanced cases.



## Results of Early Detection of Breast Cancer<sup>1</sup>

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THE Cancer Detection Center at the University of Minnesota<sup>2</sup> over its 15-year period of operation has performed annual physical examinations on 12,000 asymptomatic persons, including careful breast examination for each of the 6,000 women, 45 years or older, who have participated in the program. From 1948 through September 1958, the period for which a 5-year follow-up study can be made, 30 patients were found to have cancer of the breast.

One of these, unfortunately, had cancer of the breast already sufficiently advanced at the time of examination to preclude consideration of surgical excision and died a few weeks after diagnosis. Of the remaining 29, only 8 (28%) had microscopic involvement of lymph nodes in the subsequently excised surgical specimens. Seven of the 8 (88%) with lymph node involvement, however, survived 5 years or more following diagnosis and treatment. One of the 7 is known to have had subsequent recurrence of the cancer.

Of the 21 patients who had negative lymph nodes on microscopic examination of the surgical specimen, 20 (95%) lived at least 5 years. Two of these 20 survivors are known to have had a recurrence after 5 years, 1 dying of cancer after 7 years.

Thus, 30 patients with breast cancer detected on routine annual physical examinations at the Cancer Detection Center had an over-all "crude" 5-year survival rate of 90 percent. For 29 of these 30 patients who underwent mastectomies, the "crude" 5-year survival rate was 93 percent. Com-

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<sup>1</sup>This study was supported by the Malignant Disease Research Fund and the Donald J. Cowling Funds for Surgical Research.

<sup>2</sup>The University of Minnesota Cancer Detection Center in its early years derived partial support from the Minnesota Division of the American Cancer Society, Inc. It operates with the approval and endorsement of the Minnesota State Medical Association and its Cancer Council.

pared with usually reported over-all 5-year survival rates of about 50 percent, these figures compare very favorably and appear to represent a salvage of 80 percent of the one half or so of breast cancer patients who reportedly fail to achieve 5-year survival following diagnosis of this disease. Of some note is the observation that no patient, who detected her own breast carcinoma by self-examination, procrastinated until her next scheduled annual physical examination before seeking professional advice and therapy.

Patients who developed breast cancers not detected at the Cancer Detection Center, although active participants in the examination program (or within a year after discontinuance of participation), were also carefully followed; during the period for which 5-year follow-up could be made (1948-Sept. 1958), 14 patients were known to have developed breast cancers, detected as well as treated elsewhere than at the Cancer Detection Center. Eight of the 14 had lesions that had no evidence, on microscopic examination, of lymph node involvement in the excised specimens; all 8 patients have survived for 5 years, or longer, without evidence of recurrence. Six other patients had positive lymph nodes upon examination of the surgical specimens. One patient succumbed to a cerebral vascular accident 2 months following surgery, precluding evaluation of recurrent tumor, and one expired with recurrent cancer prior to 5-year survival. Thus, of the 14 patients in this group, 12 survived at least 5 years, for an over-all "crude" 5-year survival rate of 86 percent, which substantially exceeds usually reported survival rates.

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## Summary of General Discussion

Data available from various sources indicate that the results obtained in the treatment of breast cancer are very similar, irrespective of difference in therapeutic policy among countries and institutions. For example, the results obtained with radical surgery alone and with surgery combined with radiation were almost identical.

Since survival rates for breast cancer have been relatively stable for many years, it was suggested that increased emphasis on cancer detection may be a fruitful way to improve survival with present methods of therapy and to minimize the amount of surgery required.

There was general agreement on the need for controlled clinical trials to evaluate the relative merits of the principal treatment methods. Particularly, the simpler surgical techniques need to be compared with the more radical procedures.

The limitations of a survival rate as a specified endpoint, *e.g.*, 5 years, as a means for comparing different treatments for nonlocalized breast cancer were pointed out. By the end of the 5th year the survival curves for two methods of treatment may be close to zero, but the areas under the two curves may be significantly different. It is therefore important to use statistical measures reflecting various trends during an interval of observation, and not to base comparisons solely on "end results." The average survival time during a specified interval of observation is one method for dealing with this problem.

The discussion of leads for research on factors influencing the survival of patients with cancer of the breast included the following:

- 1) The incidence of breast cancer is much lower in Japan than in Western countries. There is some evidence that Japanese women with breast cancer have a better prognosis. Both the lower incidence rate and higher survival rate may be due to hormonal factors. Preliminary data indicate a high androgen content in the urine of Japanese women.

- 2) The change in the slope of the incidence curve (with respect to age) at the usual age of menopause suggests a hormonal effect.

- 3) A hormonal effect is also suggested by the observation that incidence rates for married and single women are different before the menopause, but are similar after the menopause.

- 4) The survival rates for women under 55 years of age and for women 55 years and over vary from country to country. It was suggested that this may be associated with a differential hormonal effect.





## **Cancer of the Ovary**

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Studies on Cancer of the Ovary in Finland, 1953-1956. CARL-ERIK UNNÉRUS,  
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## End Results Studies on Cancer of the Ovary

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CANCER register data on ovarian cancer from the United States, Norway, England, and Finland have been analyzed. In this connection the following will be discussed: the differences and the heterogeneity of tumor materials, differences in the selection of treatment, and the similarity of the end results.

### TUMOR MATERIAL

Eighty percent of ovarian tumors are benign and 20 percent malignant. It is well known that the border between malignant and benign ovarian tumor is by no means clear. The 5 most common types of malignant ovarian tumors (1, 2) are:

Serous cystadenocarcinomas	60-70 percent
Mucinous cystadenocarcinomas	15-20 percent
Carcinomas unclassified	10-20 percent
Granulosa-theca cell tumors	5-10 percent
Dysgerminomas	1-5 percent

Of these, serous and mucinous tumors are the most common: Fifty percent of the former and only 5 percent of the latter are malignant. Among the latter, there are many cases in which the question of malignancy is decided according to the examiner's concepts as to what constitutes reliable evidence of malignancy (3). If he is conservative, the percentage of all benign tumors must rise and that of localized malignant tumors fall. But if he makes a diagnosis of cancer often and only on the basis of some minor changes in the epithelium of benign tumors, then the percentage of benign tumors falls and that of localized "malignant" tumors

TABLE 1.—Cancer of the ovary. Percentage distribution, by diagnostic confirmation and stage at diagnosis, in the United States, England and Wales, Finland, and Norway

Registries and years		Total No. of cases	Percent histo- logically confirmed		Percent localized	
			All stages	Local- ized	Con- firmed	Confirmed and not confirmed
Connecticut	1945-49	597	91	98	30	28
	1950-54	743	93	99	31	29
England and Wales	1948-49	1420	76	91	26	22
	1952-53	1984	82	93	33	29
Finland	1953-56	743	78	91	52	44
Norway	1953-56	874	85	96	33	29
U.S. Central	1945-49	1369	92	99	28	26
	1950-54	1608	94	98	29	27
U.S. Teaching Hospitals	1945-49	251	93	98	25	24
	1950-54	317	93	100	22	21

risers. In granulosa cell tumors the connection between clinical malignancy and "histological malignancy" is even more uncertain. Differences in diagnosis can thus explain relatively large differences in the composition of the data and consequently also in the end results.

The percentage of *histologically* confirmed cases varied in the different materials from 76 in England and Wales in 1948-49 to 94 in the U.S. Central registries in 1950-54 (table 1). The histology of ovarian tumors in different registries could not, however, be analyzed, which is unfortunate since ovarian tumors form a very heterogeneous group.

In this connection, a study (4) of 233 serous papillary ovarian tumors from 1946-56 should be mentioned because it clearly shows how large the borderline (semimalignant) group can be. The material in question contains 123 benign tumors, 33 tumors belonging to the borderline group, and 77 malignant tumors. The tumors in the borderline group were considered as malignant and the patients were treated by surgery and radiation. All the patients survived 5 years, but 4 died of carcinoma later. One third or even more of the "malignant" ovarian tumors may thus belong to the borderline or semimalignant group.

The *extent of the disease*, when diagnosed, varied, as is shown in table 1. The high percentage of localized tumors in the Finnish material is difficult to understand and will be dealt with in more detail later on. The increase of localized tumors can, of course, result from many different factors and is not necessarily due to "earlier" diagnosis. The most important factors are the classification of benign tumors as malignant and the inclusion of not



TABLE 2.—Cancer of the ovary. Percentage distribution of confirmed cases by stage at diagnosis and age in the United States, England and Wales, Finland, and Norway

Registries and years		All stages			Localized			Not localized		
		Age groups			Age groups			Age groups		
		0-44	45-59	60-	0-44	45-59	60-	0-44	45-59	60-
Connecticut	1945-49	20	43	36	30	40	30	16	45	40
	1950-54	25	37	38	35	39	27	19	36	45
England and Wales	1948-49	23	48	28	26	52	22	13	37	50
	1952-53	20	48	32	21	44	35	11	37	52
Finland	1953-56	26	48	27	31	46	22	19	50	31
Norway	1953-56	19	47	37	24	46	30	18	47	36
U.S. Central	1945-49	22	43	36	29	41	30	18	43	38
	1950-54	22	36	42	30	40	30	18	35	47
U.S. Teaching Hospitals	1945-49	31	41	28	32	41	27	30	41	29
	1950-54	24	38	39	32	36	32	21	38	41

localized tumors in the group of localized ones. The ovarian tumors are often bilateral and the grouping of them may vary.

If not localized tumors are included in the localized group, poorer end results could be expected in the localized group, but similar end results in the whole material and the age distribution of patients with localized tumors would shift toward that of the not localized. If, on the other hand, the group of localized tumors is large, due to benign tumors being classified as malignant, then better end results would be expected in the group of localized tumors and also in the whole material, and the age distribution would shift toward that of benign tumors.

The age distribution of patients with localized and not localized tumors is shown in table 2.

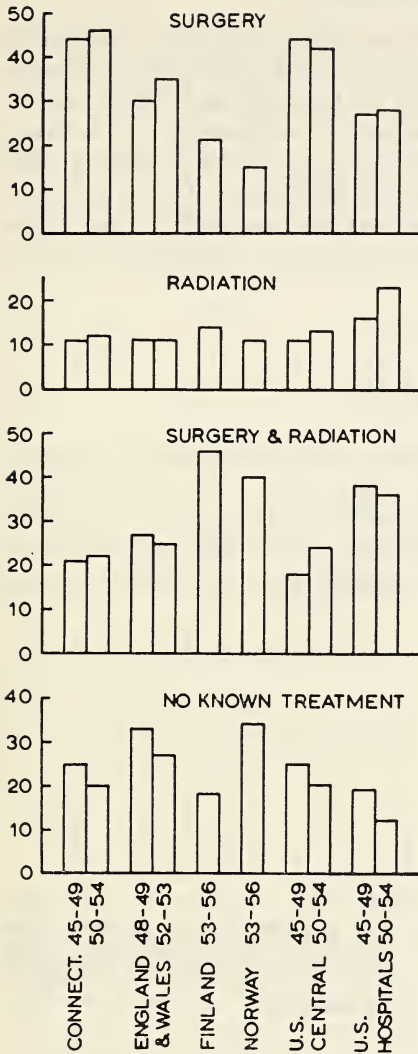
## TREATMENT

The type of treatment varied greatly in different countries (table 3 and text-fig. 1). The high percentage of patients treated by surgery alone in the United States and the exceptionally common use of combined treatment in Finland and Norway are noteworthy. It can also be noticed that the group having no known treatment decreases with time.

It is possible that the selection of treatment depends on the spread of the tumor. We examined the situation concerning surgery and surgery plus radiation using the chi-square test. The null hypothesis was that the types of treatment, *i.e.*, surgery and surgery plus radiation, are independent of the extent of the disease. The following results apply to histologi-

TABLE 3.—Cancer of the ovary. Percentage distribution of confirmed cases by treatment and age in the United States, England and Wales, Finland, and Norway

Registries and years	All cases			Surgery			Radiation			Surgery + radiation			No treatment		
	Age groups			Age groups			Age groups			Age groups			Age groups		
	0-44	45-59	60-	0-44	45-59	60-	0-44	45-59	60-	0-44	45-59	60-	0-44	45-59	60-
Connecticut	1945-49	20	43	36	23	43	34	10	44	46	25	51	24	15	35
	1950-54	25	37	38	32	35	34	14	35	51	27	50	23	8	28
England and Wales	1948-49	23	48	28	25	46	29	27	53	20	25	58	17	18	37
	1952-53	20	48	32	20	47	33	21	47	32	25	55	19	11	41
Finland	1953-56	26	48	27	30	40	30	21	51	28	26	51	23	11	48
Norway	1953-56	19	47	34	27	38	34	15	54	31	22	52	25	10	40
U.S. Central	1945-49	22	43	36	25	43	32	14	47	39	26	49	25	15	33
	1950-54	22	36	42	29	36	35	11	37	51	24	42	34	6	27
U.S. Teaching Hospitals	1945-49	31	41	28	30	39	30	35	28	26	34	47	19	21	33
	1950-54	24	38	39	26	40	35	18	39	44	28	41	31	16	19



TEXT-FIGURE 1.—Cancer of the ovary.  
Percentage distribution of different  
types of treatment.

cally confirmed cases only, but similar results were obtained also when the whole material was investigated:

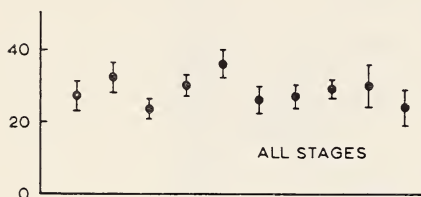
Registries		Deviation from independence
Connecticut	1945-49	Significant ( $0.001 < P < 0.01$ )
	1950-54	Significant ( $0.001 < P < 0.01$ )
England and Wales	1948-49	Not significant
	1952-53	Not significant
Finland	1953-56	Not significant
Norway	1953-56	Not significant
U.S. Central	1945-49	Significant ( $0.001 < P < 0.01$ )
	1950-54	Highly significant ( $P < 0.001$ )
U.S. Teaching Hospitals	1945-49	Possibly significant ( $0.01 < P < 0.05$ )
	1950-54	Significant ( $0.001 < P < 0.01$ )

Deviations from independence were, as expected, in the direction of treatment of localized cases by surgery alone and not localized cases by surgery plus radiation. The situation in England and Wales and in Finland and Norway where no such selection was observed is of interest.

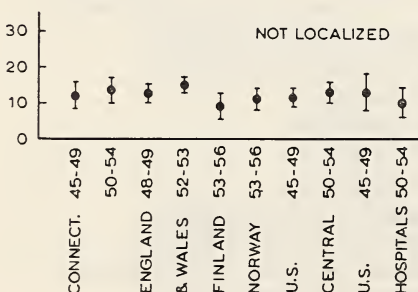
The situation in Finland could probably be explained by assuming that, due to long distances and the few hospitals with good radiation facilities, "hopeless" cases with distant metastases are often treated by surgery alone and are not referred to the central hospitals for postoperative X-ray treatment.

## END RESULTS

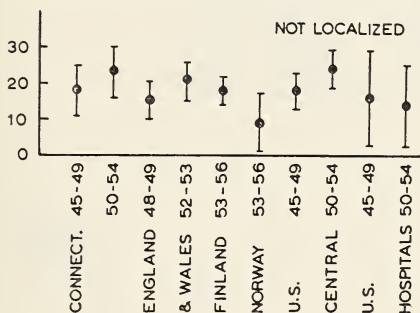
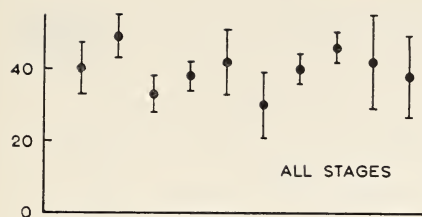
As seen in the survival summary tables and in text-figures 2, 3, and 4, the end results are very similar in all studies. The *extent of the disease*, of course, greatly influences the end results; in the group of localized tumors the 5-year survival rate varied from 0.53 to 0.80 and in the not localized group from 0.09 to 0.13. In studies of more localized tumors



TEXT-FIGURE 2.—Cancer of the ovary. The relative 5-year survival rates (with 95% confidence intervals) of confirmed cases by stage at diagnosis. All treatments.







TEXT-FIGURE 3.—Cancer of the ovary. The relative 5-year survival rates (with 95% confidence intervals) of confirmed cases by stage at diagnosis. Surgery.

the end results should thus be much better. This hypothesis has been tested by studying the correlation between the end results and the stage of disease (text-fig. 5). The regression line has been calculated by using as weights the number of cases by each observation point.

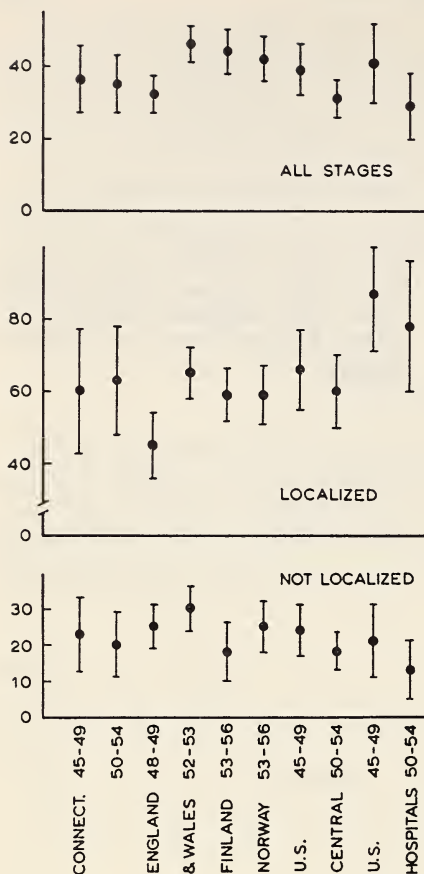
The estimate of the regression of the end results of all cases on the percentage of localized cases was:

$y = 16.18 + 0.3873 x$ , where  $y$  = relative 5-year survival rate of all cases, and  $x$  = percent of localized cases.

The coefficient, 0.3873, differs significantly from zero, *i.e.*, correlation exists.

We also studied (text-fig. 6) the survival rate of cases with localized tumor, as the data containing more localized cases might be better. This could indicate that the localized group also included benign tumors. The regression line was calculated as before:

$y = 63.55 - 0.0745 x$ , where  $y$  = relative 5-year survival rate of localized cases, and  $x$  = percent of localized cases.



TEXT-FIGURE 4.—Cancer of the ovary. The relative 5-year survival rates (with 95% confidence intervals) of confirmed cases by stage at diagnosis. Surgery and radiation.

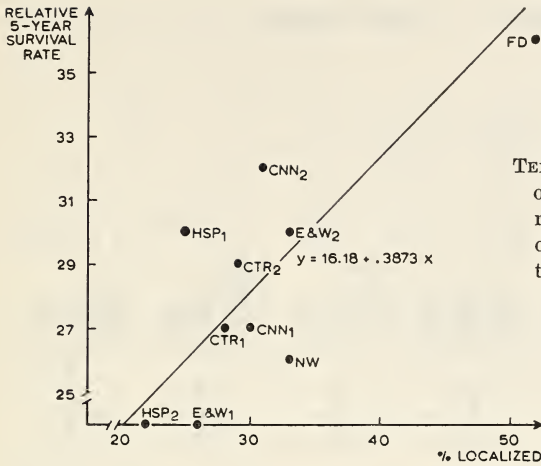
The coefficient, 0.0745, does not differ significantly from zero value, which means that the results do not justify conclusions as to the possible existence of a correlation. The increase of localized tumors does not seem to result solely from treating benign tumors as malignant. Some not localized tumors are probably also included in the localized group.

The results are very similar also when the not confirmed cases are added to the group of the histologically confirmed.

The *age distribution* of the confirmed cases by treatment is shown in table 3.

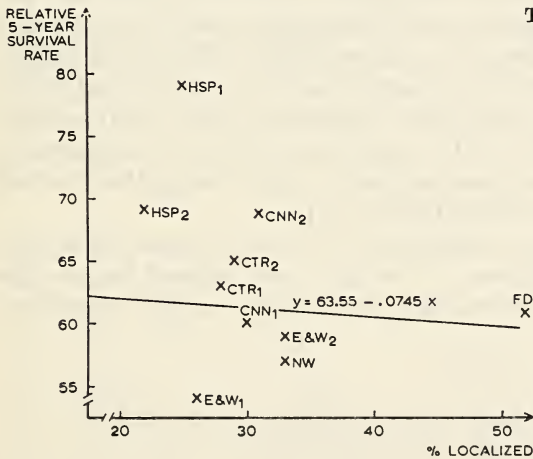
The results of treatment seem to be better in the younger age groups, which confirm earlier results (5) (text-fig. 7).

However, as is seen in text-figure 8, the younger age groups also contain fewer untreated cases and more localized cases. Even if the results are given by stage, as in text-figure 7, it is likely that the not localized group at older ages contains more cases with very diffuse and remote metastases than the corresponding group at younger ages.



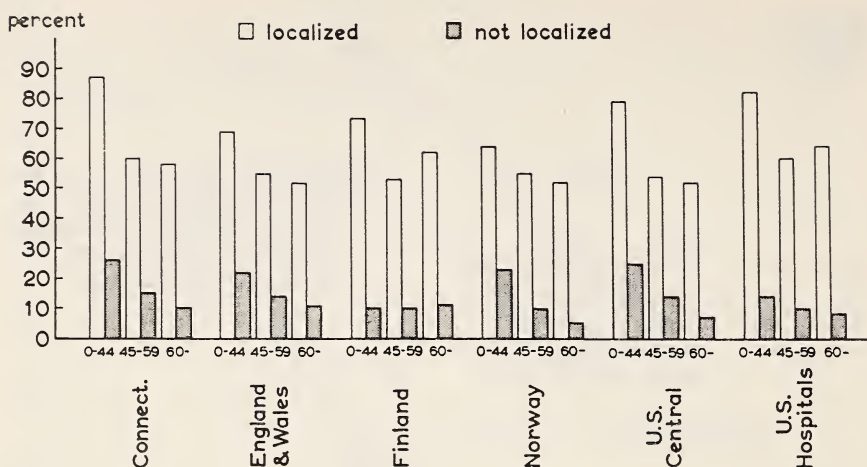
TEXT-FIGURE 5.—Cancer of the ovary. Confirmed cases. Correlation between the percentage of localized cases and the relative 5-year survival rate.

CNN <sub>1</sub> = CONNECTICUT	45 - 49
CNN <sub>2</sub> = CONNECTICUT	50 - 54
E&W <sub>1</sub> = ENGLAND & WALES	48 - 49
E&W <sub>2</sub> = ENGLAND & WALES	52 - 53
FD = FINLAND	53 - 56
NW = NORWAY	53 - 56
CTR <sub>1</sub> = U.S.CENTRAL	45 - 49
CTR <sub>2</sub> = U.S.CENTRAL	50 - 54
HSP <sub>1</sub> = U.S.HOSPITALS	45 - 49
HSP <sub>2</sub> = U.S.HOSPITALS	50 - 54



TEXT-FIGURE 6.—Cancer of the ovary. Confirmed cases. Correlation between the percentage of localized cases and the relative 5-year survival rate of localized cases.

CNN <sub>1</sub> = CONNECTICUT	45 - 49
CNN <sub>2</sub> = CONNECTICUT	50 - 54
E&W <sub>1</sub> = ENGLAND & WALES	48 - 49
E&W <sub>2</sub> = ENGLAND & WALES	52 - 53
FD = FINLAND	53 - 56
NW = NORWAY	53 - 56
CTR <sub>1</sub> = U.S.CENTRAL	45 - 49
CTR <sub>2</sub> = U.S.CENTRAL	50 - 54
HSP <sub>1</sub> = U.S.HOSPITALS	45 - 49
HSP <sub>2</sub> = U.S.HOSPITALS	50 - 54

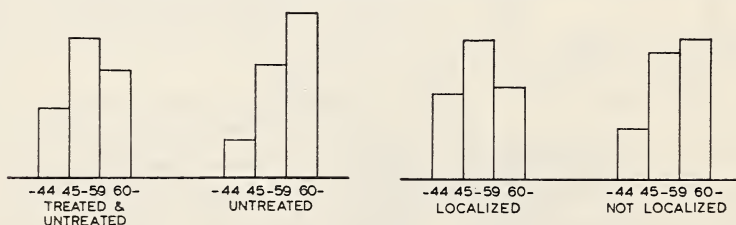


TEXT-FIGURE 7.—Cancer of the ovary. The relative 5-year survival rates of confirmed cases by age and stage at diagnosis.

It should also be remembered that the mean age of cases with benign ovarian tumors is lower than that of malignant tumors, and the borderline (or semimalignant) group is in this respect indistinguishable from the benign group. Thus the results do not necessarily indicate that malignant tumors are less malignant in younger than in older groups or that the treatment is more effective in these age groups.

In this connection we will refer to an aspect of some theoretical interest. The situation illustrated previously will change somewhat if the mortality due to cancer alone is considered, *i.e.*, the probability of dying both from cancer and from other causes is subtracted from the probability of dying from cancer, which is not done in the calculation of the usual relative survival rate. The probability of the complement of this excess mortality (of the survival) in a given cancer population is the sum of the observed survival rate and the expected mortality rate (6).

The effect of this method is illustrated with the use of the data from England and Wales and Norway. The data were selected because the relative survival rates in different age groups show an even regression.



TEXT-FIGURE 8.—Cancer of the ovary. Percentage distribution of confirmed cases by age. All registries combined.

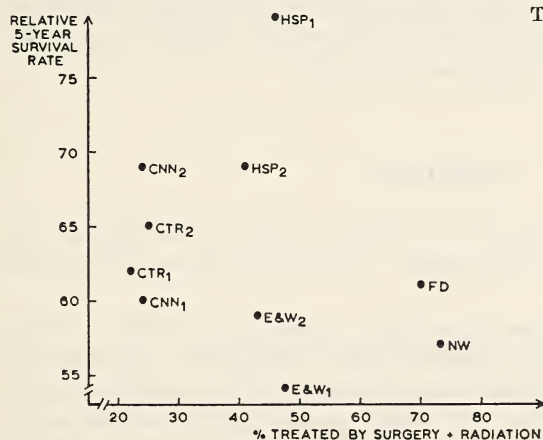


The figures include the histologically confirmed cases only.

	Five-year relative survival rate in different age groups			Five-year survival rate concerning cancer alone in different age groups		
	0-44	45-59	60 and over	0-44	45-59	60 and over
England and Wales	44	28	23	44	32	37
Norway	40	25	20	40	27	33

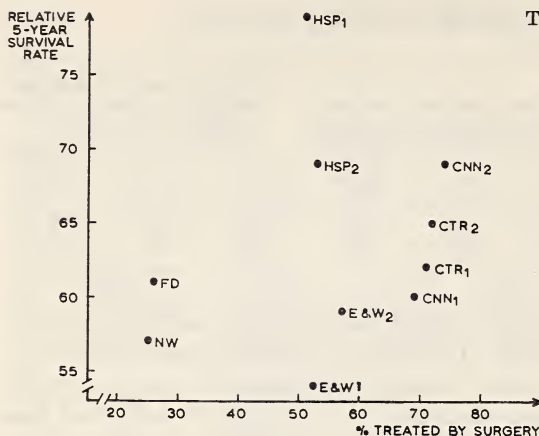
Survival rates for cancer alone are relatively near each other in the youngest and oldest age groups. The small residual difference may be explained to a great extent by the facts mentioned earlier and by random variations. Thus, the results obtained by the method described here seem to be more in accordance with the clinical experience than the data of relative survival rates.

The possible effect of the *different types of treatment* on the 5-year survival rates was preliminarily studied, but no conclusions about the significance of the differences could be made. As is well known, opinions on the justification of postoperative X-ray treatment are divergent. In the light of the present material the value of X-ray treatment is still open to question (text-figs. 9 and 10). The possible correlation may have been disturbed by other variables. As mentioned earlier the treatment (surgery or surgery plus radiation) is selected in the United States by the



TEXT-FIGURE 9.—Cancer of the ovary. Confirmed and localized cases. Correlation between the percentage of cases treated with surgery and radiation and the relative 5-year survival rate.

CNN<sub>1</sub> = CONNECTICUT 45-49  
 CNN<sub>2</sub> = CONNECTICUT 50-54  
 E&W<sub>1</sub> = ENGLAND & WALES 48-49  
 E&W<sub>2</sub> = ENGLAND & WALES 52-53  
 FD = FINLAND 53-56  
 NW = NORWAY 53-56  
 CTR<sub>1</sub> = U.S.CENTRAL 45-49  
 CTR<sub>2</sub> = U.S.CENTRAL 50-54  
 HSP<sub>1</sub> = U.S.HOSPITALS 45-49  
 HSP<sub>2</sub> = U.S.HOSPITALS 50-54



TEXT-FIGURE 10.—Cancer of the ovary. Confirmed and localized cases. Correlation between the percentage of cases treated with surgery and the relative 5-year survival rate.

CNN <sub>1</sub>	= CONNECTICUT	45-49
CNN <sub>2</sub>	= CONNECTICUT	50-54
E & W <sub>1</sub>	= ENGLAND & WALES	48-49
E & W <sub>2</sub>	= ENGLAND & WALES	52-53
FD	= FINLAND	53-56
NW	= NORWAY	53-56
CTR <sub>1</sub>	= U.S. CENTRAL	45-49
CTR <sub>2</sub>	= U.S. CENTRAL	50-54
HSP <sub>1</sub>	= U.S. HOSPITALS	45-49
HSP <sub>2</sub>	= U.S. HOSPITALS	50-54

extent of the tumor. Thus, even when we consider only localized tumors, it can be expected that inside that group there exists selection in the same direction, even if this is impossible to see. The tumor might be more or less localized. Thus, the observed differences can be explained by factors other than those studied. Conclusions concerning the effect of different types of treatment on the end results are not justified without a very exact analysis of the figures and perhaps not even then.

## SUMMARY

Cancer register data from the United States, England and Wales, Finland, and Norway have been analyzed. The total study comprises 8,566 cases.

The heterogeneity of ovarian tumor data in general is stressed. Differences in diagnosis can explain relatively large differences in the composition of data from various countries and consequently also differences in the end results of these studies. The high percentage of cases treated by surgery alone in the United States and the common use of combined treatment in Finland and Norway are noteworthy. The percentage of localized cases varied greatly in the different data. In the United States, localized tumors are treated by surgery alone and not localized tumors usually by combined treatment. No such selection of treatment was observed in the data from England and Wales, Norway, and Finland.

The end results in all studies were very similar. The possible effect of different types of treatment on the 5-year survival rates was examined, but no conclusions about the significance of the observed differences could be made. The value of X-ray treatment for localized ovarian tumors remains open to question.

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## **Studies on Cancer of the Ovary in Finland, 1953-1956**

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X-Ray Department, University Central Hospital,  
Departments of Obstetrics and Gynecology, Hel-  
sinki, Finland*

IN most publications ovarian carcinomas are dealt with as one group under the same heading. However, Munnell and Taylor note that ovarian carcinoma is not a separate disease but rather a group of diseases and stress that in research it is more useful to concentrate on some histogenetically known type than on the whole heterogeneous group comprising ovarian carcinomas.

Because it is sometimes impossible to determine by microscopic examination whether a growth is malignant, expressions like semimalignant or borderline tumors, potentially malignant or suspicious tumors have been used. Since there is no clear definition of the types included in this group, the opinions of competent pathologists may often vary. Woodruff and Novak, 1954, mention that in the highly authoritative 5-member Committee (The Ovarian Tumor Registry), which classified material, there were several instances in which the members differed when the issue concerned borderline tumors.

More than one third of all patients with ovarian cancer in Finland are treated at the Women's University Hospital, in which there are two clinics, each headed by a professor. The clinicians may differ in the indications for surgical or other treatment. However, for both clinics there is the same pathologist, a "professor competent" in gynecology and pathology. I have been responsible for the radiation therapy and, in consultation with the clinicians, for all the general cancer therapy. An effective follow-up system has existed for over 40 years in the hospital.

Because the treatment is based on the diagnoses of the clinicians and the pathologist, it is important to know how these specialists arrive at their diagnoses. Vara and Pankamaa analyzed the ovarian cancer operations in this hospital during 1900-44. From histological findings they classified

1,149 ovarian tumors. Slides have been kept since 1923, and hence histological re-evaluation has been possible in 77 percent of the cases. There were 565 epithelial tumors (49%), of which 344 were benign and 221 (39%), malignant.

I mention this as an indication of how much views have changed in the course of time and how manifestly a more accurate mode of diagnosis has gradually been reached. The greatest difficulties still arise over whether the tumor is benign or malignant.

Serous papillary ovarian tumor is a good example. In 1963, using the classification accepted at the International Congress in Vienna, Purola collected 233 cases of this type from the material in our hospital and divided them according to the histological form or grade:

Grade I. Benign papillary cystadenoma, inactive type

Grade II. More active, hyperplastic type of benign papillary cystadenoma

Grade III. Borderline group

Grade IV. Well-differentiated cystadenocarcinoma; malignant changes clear

Grade V. Anaplastic, poorly differentiated cystadenocarcinoma

Purola placed 41.6 percent of the cases in group I, 11.3 percent in group II, and 14.2 percent in group III—the borderline group. The really malignant cases were group IV with 18.7 percent and group V with 14.2 percent. Thus about one third were malignant.

It is worth recalling here the clinical stage classification recommended by the Cancer Committee of the International Federation of Gynecology and Obstetrics at the Vienna Congress in 1961:

Stage I. Growth limited to the ovaries (one or both)

Stage II. Growth involving one or both ovaries with pelvic extension

Stage III. Growth involving one or both ovaries with widespread metastases, but partially removable

Stage IV. Growth involving one or both ovaries; entirely inoperable

It is interesting to analyze the 233 cases of serous papillary ovarian tumors for the correlation between the clinical stage of disease and the histological type of tumor (table 1.). The tumors of Grades III and IV were limited in most cases to the ovaries. In Grade V, however, over half comprised tumors which had already spread outside the pelvic area. No patient with a tumor belonging to the histologically benign group, Grades I and II, and to the borderline type, Grade III, died of cancer. The prognosis in the well-differentiated carcinoma group (absolute 5-year survival rate, 55%) was distinctly better than that in the anaplastic group,

TABLE 1.—Clinical stage of disease according to histological type of tumor (Purola)

Histological grade	Number of patients	Stage:			
		I	II	III	IV
III	33	24	5	2	2
IV	44	24	11	4	5
V	33	7	6	11	9

in which only 15 percent of the patients were living after 5 years. The difference is statistically highly significant.

It is said that, in principle, the treatment for ovarian cancer is always surgical. I will not discuss the differences in the operative methods, but I think it worthwhile to emphasize that one can never talk about pure radical operation of ovarian cancer. The extent to which radiotherapy is indicated in patients with ovarian cancer has been similarly debated. The radiotherapy applied takes into account the histological diagnosis, spread of the tumor, general condition, etc. We used the following treatments during 1953–56:

(a) localized cases: 1) operation, 2) postoperative radiotherapy, and 3) hormones and general treatment

(b) possible local spread: 1) often preoperative radiotherapy, 2) operation, 3) postoperative radiotherapy, and 4) hormones and general treatment.

(c) generalized spread when primary site is unknown: 1) laparotomy (if possible), 2) radioactive gold ( $\text{Au}^{198}$ ), in two or three sessions, and 3) finally, radiotherapy to the sites of possible metastases

Table 2 shows number of operations performed in our hospital from 1919–56. Attention is drawn to the considerable increase in the number of operations, especially in 1949–56, which is partly the result of improved surgical facilities. This is reflected in the considerable drop in primary mortality. On the other hand, the 5-year recovery rate has decreased slightly in the last group, and it may be asked whether surgery has been used too frequently.

TABLE 2.—Ovarian cancer: treatment and results\*

Calendar period	Number of patients	Number of operations	Primary deaths during operation (%)	Symptom-free after 5 years (%)
1919–33	151	82 (55.8%)	7.3	17.8
1934–48	286	151 (52.8%)	3.2	36.3
1949–56	284	190 (66.9%)	2.6	32.6

\*Patients with metastatic cancer are excluded



Our radiotherapy probably differs a little from that used in other countries. Since the middle of 1953 we have used moving-beam X-ray therapy in most cases and have thus avoided damage to the skin while the desired depth dose is reached. The guide for modern radiotherapy must be what is termed "isodose thinking," which means that we seek to create individual treatment fields so that the tumor of every patient is "ringed" by the correct isodoses.

Our treatment is more fractionated than in many other European hospitals; the total course of treatment can take up to half a year, or even longer. The total depth dose must be at least 3000 r. Why should we use a lower dose in this type of cancer than in others? I believe that the good or poor result of radiotherapy depends on this.

Since 1958 we have used  $\text{Au}^{198}$  in over 100 patients. The results at first appeared to be rather discouraging, but this was chiefly because at the outset the patients selected were almost exclusively those in which the treatment was only palliative. But when we began to give the treatment also to patients who were less ill and suspected to have free cancer cells in the abdominal cavity, *i.e.*, after operation, the significance of this therapeutic method increased. I consider that  $\text{Au}^{198}$  or some other suitable radioactive isotope is fairly effective in the treatment of certain patients with ovarian cancer.

Frequently inoperable cases have been made operable after fractionated radiotherapy. Opinions on the justification of postoperative X-ray treatment are divergent. Most clinicians regard it as an absolute complement to surgical treatment, but some question its value. I believe that the explanation for these negative viewpoints is partly that radiotherapy has not been administered adequately and partly that it has not been correlated with the histological diagnosis—a correlation that we always make. I try in this way to choose from among many different therapeutic methods and combinations of methods the most suitable for each patient. There are many shades of emphasis even in radiotherapy, and the range of combinations with other therapeutic methods is broad. Indeed, use of the term "radiotherapy" alone is not always advisable, for the procedure now embraces so many different forms.

As long as there is a shortage of doctors in Finland, we must look critically at the results from some of the country hospitals. In the past sufficient biopsies were not taken, especially from the more distant lymph nodes, for a really accurate assessment.

In the Women's University Hospital I have treated most of the patients as if the tumors were more generalized than the clinicians believed. Therefore, I have generally followed the diagnosis of the pathologist. I have also given the less radiosensitive patients a longer fractionating treatment, which resulted in a higher total dose. It is important not to forge ahead with radiotherapy without consideration of the patient's gen-



eral condition. The treatment must be interrupted when necessary and hormones and general treatment given instead.

It can be said with truth that the whole treatment is based on the histological diagnosis, and therefore nearly everything depends on the pathologist's opinion. The fact that in Finland so many cancers are reported as localized may be attributed to too few biopsies, an indirect result of a lack of doctors. It is also due to the long distances the patients have to travel.

Ovarian cancers have always been a special group in which the estimation of the degree of malignancy is, in part, subjective. In our older material, about 15 to 20 percent were cases in which there was some doubt as to whether the tumors were malignant or semimalignant. It is seldom possible to draw a hard and fast dividing line between them, but it would be of future benefit to establish cooperation across frontiers, and, even more, within the boundaries of our own countries, so that histological examinations are made by several pathologists who could also form small groups to submit opinions on especially difficult diagnoses. Perhaps we will have to add some special biochemical methods to assure earlier diagnosis of ovarian tumors. Even now there seem to be different biochemical reactions when the histological picture indicates the same diagnosis in two cases.

The borderline group of ovarian tumors poses a real problem. It will hardly ever be possible to make a completely reliable finding unless a considerably greater number of serial sections from each tumor are examined, but it will be a long time before there is sufficient staff available or trained for such examinations. "Borderline group" seems to be more appropriate than "semimalignant."

Clinicians, pathologists, and radiotherapists should all have a wider knowledge to appreciate each others' problems. Our attempts to encourage this mutual information in the Women's University Hospital in Helsinki have influenced our results favorably.

To conclude, I wish to emphasize that even when an ovarian tumor appears to be localized, because of its character it is quite often disseminated. That is one reason for our comprehensive scheme of treatment of malignant tumors. But the first thing that should be achieved internationally is cooperation between pathologists in the exchange of specimens. Only when it is known with certainty that the same "language" is used in similar cases will it be possible to compare more seriously the therapeutic results of different countries. When that point has been reached, it would be rational to get groups of physicians together—as has been done now—to reanalyze the question of ovarian tumor diagnosis. As far as I can see, this international organization is an excellent forum in which to bring forward such suggestions for improvement in diagnosis and treatment

and, in addition, to work for their realization. This is of the greatest significance both for practical medicine and especially for the deeper aims of research.

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### **Summary of General Discussion**

There was general agreement on the enormous difficulties involved in classification of malignant disease of the ovary. This site has a wide range of tumors from benign to highly malignant and it is doubtful whether certain tumors found in the ovary originate in that site. Furthermore, the conventional histologic criteria now in use do not correlate well with the biological characteristics of the tumor as measured by patient survival.

The need for a fresh approach to the classification of ovarian tumors was suggested. Comparative descriptions of tumors in patients experiencing short and long survival after treatment could be undertaken in a systematic search for characteristics which may provide better discrimination among tumors and be more useful prognostic indicators.

Dr. Wangenstein reported on the value of the "second-look" operation in prolonging life. This was exploratory surgery done at the time of follow-up, which enabled the detection and removal of early secondary spread not discernible by ordinary clinical examination.





## **Cancer of the Prostate**

End Results in Cancer of the Prostate. L. LIPWORTH, England

### GENERAL DISCUSSION

Moderator

ERKKI SAXÉN, Finland

Rapporteur

ANNA HOUGEN, Norway

Discussants

WILLIAM M. HAENSZEL, USA

J. L. HAYWARD, England

CALVIN ZIPPIN, USA

Presented at the International Symposium on End Results of Cancer Therapy,  
Sandefjord, Norway, September 16-20, 1963.



## End Results in Cancer of the Prostate

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THE true incidence of carcinoma of the prostate is difficult to ascertain. Most common in the elderly, already prone to fatal circulatory and other diseases, its presence is often unsuspected, as necropsy surveys have shown. In the five countries, the United States, France, Finland, Norway, and England and Wales, presenting cancer registration figures for the years 1952-56, the crude death rates due to prostatic malignancy varied from 73 to 197 per million population.

The statistics supplied by the registries of these five countries, derived largely from registrations in varying periods from 1950-56,<sup>1</sup> show that the percentage of cases of carcinoma of the prostate that were confirmed by biopsy ranged from 41 percent in Finland to 76 percent in the U.S. Central registry (table 1). No separation into "confirmed" and "not confirmed" was made in the French tabulations.

TABLE 1.—Percentage of cases confirmed by histology in the separate registries\*

Registries	1945-49	1950-56
England and Wales	43	51
Finland	—	41
Norway	—	60
U.S. Central	73	76
Connecticut†	75	76
U.S. Hospital	60	63

\*Comparison of percentage confirmed in England and Wales registry before 1950 with percentage in 1952-53 significant ( $P<0.01$ ). Comparison between England and Wales and other registries significant ( $P<0.01$ ). Comparison between Finnish and all other registries significant ( $P<0.01$ ).

†The Connecticut registry returns are included in those of the U.S. Central registry but are shown separately because of completeness of coverage in Connecticut.

<sup>1</sup> Registrations for 1945-49 were also analyzed for the England and Wales and the U.S. registries, and the results are compared briefly with the later results in these registries in the section on End Results.

The patients shown in the French register were notified during 1945-57.

TABLE 2.—Percentage of cases confirmed by histology shown for all stages, localized cases, and patients treated by chemohormones or surgery

Registries		All stages	Localized	All stages	
				Chemo-hormones	Surgically treated
England and Wales	1952-53	51	68	13	85
Finland	1953-56	41	55	20	70
Norway	1953-56	60	74	23	99
U.S. Central	1950-54	76	89	35	93
Connecticut	1950-54	76	91	27	88
U.S. Hospital	1950-54	63	73	33	92

The immense difference between the proportionate amount of histology done in surgically treated patients and those given chemotherapy or hormones only, as shown in table 2, makes it advisable, when discussing incidence, to consider all cases whether confirmed or not confirmed. In some aspects of the end results of treatment, however, a breakdown based on the presence or absence of histological confirmation will be used.

### AGE DISTRIBUTION

The proportion of patients aged 70 years and older was roughly 60 percent in the England and Wales and the U.S. Central registry. In Norway, where the death rate for cancer of the prostate is the highest of the five participant countries, the proportion of older men was 69 percent, while in Finland, with the lowest death rate for this neoplasm, the proportion of men 70 years and older was only 51 percent. It is thus obvious that the excess of prostatic cancer in Norway is largely confined to the older groups (table 3). This is also evident on examination of Norwegian and Finnish

TABLE 3.—Percentage of patients 70 years of age and older in the participant registries 1945-49 and 1950-56, confirmed and not confirmed cases\*

Registries	Percentage 70 years and older	
	1945-49	1950-56
England and Wales	53	59
Finland		51
Norway		69
U.S. Central	61	61
Connecticut	62	61
U.S. Hospital	49	50
France (1945-57)	39	

\*Comparison between percentage of patients 70 years of age and older in France with 1950-56 figures of other registries significant ( $P<0.01$ ). Comparison between Finland or U.S. Hospital registry and other registries statistically significant ( $P<0.01$ ). Comparison of age distribution in England and Wales before and after 1950 significant ( $P<0.01$ ).



mortality tables relating to this condition. The percentage 70 years of age and older in the French register was only 39 percent. This is probably due to selection and will be considered in the discussion on stage distribution.

### EXTENT OF SPREAD

Accumulation of all the 1950-56<sup>2</sup> data of the participant registries show that almost 50 percent of cases were considered to be localized when patients were treated. In the England and Wales figures, however, only 41 percent of all cases were in this category in the corresponding period making statistically significant differences ( $P < 0.01$ ) with the U.S. Central registry in both age groups separately. This may be due partly to different methods of staging, but the more likely explanation is that at the time of these registrations in England and Wales, cancer coverage was virtually complete in radiotherapy institutions and limited elsewhere, thus showing a large number of patients with more advanced disease (table 4).

As this bias toward patients seen at radiotherapy centers was much more marked in 1948-49 than in 1952-53, the highly significant differences in the proportions of patients with localized disease in these two periods in England and Wales are not surprising.

TABLE 4.—Percentage of localized cases shown in two age groups in 1945-49 and 1950-56, confirmed and not confirmed

Registries	Under 70 years		70 years and older	
	1945-49	1950-56	1945-49	1950-56
England and Wales	27	40	30	42
Finland		53		53
Norway		58		59
U.S. Central	47	52	47	48
Connecticut	50	54	56	51
U.S. Hospital	35	44	41	49
France (1945-57)	31		50	

In the French figures the percentage of the younger patients with localized growths was significantly less than that in patients 70 years of age and older (31 and 50%, respectively). As the registrations in France are derived largely from centers specializing in the treatment of cancer, a similar selection of cases to that described in England and Wales may be operative, making it difficult to draw any definite conclusions, regarding stage as well as age distribution.

Examination of the two age groups separately shows no effect of age on the degree of spread of the disease. A more detailed age and stage

<sup>2</sup> France, 1945-57.

breakdown is necessary to confirm findings described in the Registrar General's Statistical Review for England and Wales, 1952, Supplement on Cancer, based on England and Wales registrations in 1945-49, that metastases in prostatic carcinoma are more common in younger patients and local invasion in older age groups.

### CHOICE OF TREATMENT

In localized cases of prostatic cancer, surgery was the usual treatment. Operative treatment was employed in 77 percent of the early cases in the U.S. Central registry and in 60 to 70 percent of these patients in the figures of England and Wales, France, and Norway. In Finland the corresponding figure was 46 percent, but a further 11 percent of the patients had surgery followed by radiation, a combination used only in negligible proportions of early growths elsewhere.

Undoubtedly, many of the surgically treated patients were subsequently given estrogens.

The Scandinavia and England and Wales registries used one of the many forms of hormonal treatment, or occasionally chemotherapy, in 23 to 30 percent of their localized growths. In the large U.S. Central registry,

TABLE 5.—Percentage of patients given various forms of therapy—all ages—1950-56, confirmed and not confirmed cases

Localized						
Registries		Surgery	Radiation	Surgery and radiation	Chemotherapy/hormone	No known treatment
England and Wales	1952-53	70	1	1	23	4
Finland	1953-56	46	3	11	30	10
Norway	1953-56	63	4	2	23	8
U.S. Central	1950-54	77	0	1	8	14
Connecticut	1950-54	81	0	1	5	13
U.S. Hospital	1950-54	60	1	0	33	6
France*	1945-57	59	—	—	—	—
Not localized						
England and Wales	1952-53	34	7	1	41	18
Finland	1953-56	17	11	5	39	28
Norway	1953-56	13	8	1	58	20
U.S. Central	1950-54	48	3	2	27	19
Connecticut	1950-54	64	1	2	12	20
U.S. Hospital	1950-54	38	3	1	49	9
France*	1945-57	23	44	—	—	—

\*The methods of treatment analyzed in the French returns are confined to those where numbers are sufficient to be of statistical value.

on the other hand, only 8 percent had this form of treatment, but in the U.S. Hospital figures, derived from several teaching hospitals and a large radiotherapy center, the proportion was 33 percent. Here again, selection may have been a factor affecting the type of case sent to teaching institutions.

Radiation therapy without surgery was used in 3 to 4 percent of patients with early neoplasm in Finland and Norway, but rarely elsewhere.

In the advanced cases both surgery and chemotherapy or hormonal treatment was commonly used, the former predominating in the U.S. Central registry figures and the latter in the European. The U.S. Hospital registry again followed the European pattern with 49 percent of the patients with not localized cancer receiving chemotherapy or hormones and 38 percent undergoing surgery.

Radiation therapy was used in 44 percent of the French and in 11 percent of the Finnish patients with advanced growth, and in still smaller numbers in the other registries. Limitation of registration in France to anticancer centers would undoubtedly account for part of the high percentage of patients with advanced cancer treated by radiation. Treatment methods were essentially similar for patients in the two age groups studied (under 70, 70 years, and older).

#### END RESULTS 1950-56 (FRANCE 1945-57)

Carcinoma of the prostate appears to have a fair prognosis for an internal cancer, one fourth of all patients surviving 5 years, with a corrected survival for this period of about 38 percent. In the figures provided, the mortality was highest in the first year after treatment, when almost as many deaths occurred as in the subsequent 4 years.

Considering the results for all ages and degrees of spread of the neoplasm (table 6), the 5-year corrected survival varied from 22 percent in the French and 23 percent in the Finnish to 40 percent in the U.S. Central registry. The difference between the French or Finnish figures and that of the 1950-56 registrations of any other registry was highly significant ( $P < 0.01$ ), while in England and Wales the 34.4 percent corrected survival was also significantly below that of the U.S. Central registry ( $P < 0.01$ ).

Turning to the separate stages (tables 7A and B), the 5-year corrected survival for localized growths is about 60 percent for cases below 70 years of age and 47 percent in the older patients, so that age appeared to affect the prognosis in early malignancy to a marked extent. Here again the corresponding Finnish registry results of 38 percent and 36 percent in the younger and older age groups, respectively, were both significantly less than that of the U.S. Central registry, where the 5-year corrected survival



TABLE 6.—Five-year corrected survival rates (%) for all ages and stages of disease, confirmed and not confirmed cases

Registries	1945-49	1950-56
England and Wales	30.3 $\pm$ 3.0*	34.4 $\pm$ 2.6*
Finland		22.9 $\pm$ 4.0
Norway		37.6 $\pm$ 2.9
U.S. Central	36.0 $\pm$ 2.4	39.8 $\pm$ 2.2
Connecticut	35.3 $\pm$ 3.7	41.0 $\pm$ 3.4
U.S. Hospital	37.6 $\pm$ 5.7	41.9 $\pm$ 5.1
France (1945-57)	21.7 $\pm$ 6.4	

\*Two standard errors.

was 61 percent in the younger patients and 51 percent in those over 70 years of age ( $P < 0.01$ ). Equally, the experience of the older patients with localized disease in the French register, where the corrected 5-year survival was only 25 percent, differed significantly from that of the same group in the U.S. Central registry ( $P < 0.01$ ). In the advanced cases results were not as much affected by age, the 5-year corrected survival for these patients being about 20 percent. Here again in Finland the comparatively poor survival of 7 percent in both age groups was significantly lower than that in the United States, England and Wales, and Norway registries.

The variations between the different registries in these results might possibly be due to the inclusion of different proportions of comparatively benign "latent" prostatic carcinoma discovered on section after surgery for nonmalignant conditions. However, this would not apply to the advanced cases, and examination of cases not confirmed histologically reveals the same differences in the Finnish results (table 8). As previously mentioned no breakdown into "confirmed" and "not confirmed" is shown in the French data.

It is also apparent that, though these contrasts between the Finnish and other registries were found in both age groups, they are more marked in the younger patients.

## RESULTS WITH DIFFERENT FORMS OF TREATMENT

### Surgery

The results after surgery were superior to those for all treatments combined in both stages of the disease. The exceptions were the younger patients in England and Wales with localized disease, and the same age group with advanced disease in Finland. The better survival after surgery could be due to selection, a higher incidence of "latent" prostatic cancer among the early growths, and the fact that many of the surgically treated patients undoubtedly had hormone therapy later.



TABLE 7A.—Five-year corrected survival rates (%), by stage of disease, patients under 70 years of age

Registries	1945-49			1950-56		
	All stages	Localized	Not localized	All stages	Localized	Not localized
England and Wales	36.2 ± 4.0*	65.8 ± 8.5	19.6 ± 4.1	38.9 ± 3.6	64.9 ± 6.2	21.9 ± 3.8
Finland	No figures available before 1950			23.4 ± 5.1	37.5 ± 8.4	7.0 ± 4.5
Norway				42.9 ± 4.6	60.4 ± 6.4	16.0 ± 5.5
U.S. Central	34.8 ± 3.3	49.7 ± 5.3	17.6 ± 3.9	43.4 ± 3.2	60.6 ± 4.7	21.8 ± 4.2
Connecticut	34.8 ± 5.2	45.8 ± 8.0	19.3 ± 6.7	47.3 ± 4.9	63.0 ± 6.8	22.8 ± 6.8
U.S. Hospital	37.1 ± 7.1	62.7 ± 13.0	15.5 ± 7.2	43.1 ± 6.5	64.5 ± 10.2	21.1 ± 8.1
France (1945-57)	—	—	—	23.3 ± 7.8	46.0 ± 17.2	13.5 ± 9.0

\*Two standard errors.

TABLE 7B.—Five-year corrected survival rates (%), by stage of disease, patients 70 years of age and older

Registries	1945-49			1950-56		
	All stages	Localized	Not localized	All stages	Localized	Not localized
England and Wales	22.6 ± 4.1*	41.5 ± 9.9	12.4 ± 3.9	29.7 ± 3.6	44.4 ± 6.5	18.8 ± 3.9
Finland		No figures available before 1950		22.1 ± 6.4	35.5 ± 10.7	6.8 ± 6.0
Norway	37.1 ± 3.4	48.1 ± 5.6		34.2 ± 3.7	45.5 ± 5.5	14.1 ± 4.5
U.S. Central	35.8 ± 5.2	43.0 ± 7.5	22.4 ± 4.5	36.8 ± 3.1	51.2 ± 5.1	19.5 ± 3.8
Connecticut	38.4 ± 9.2	50.0 ± 15.5	21.0 ± 7.0	35.3 ± 4.7	47.5 ± 7.3	20.6 ± 6.2
U.S. Hospital			23.5 ± 11.6	40.3 ± 8.3	52.9 ± 13.3	21.0 ± 10.5
France (1945-57)	—	—	—	18.3 ± 11.2	24.8 ± 16.8	14.6 ± 16.2

\*Two standard errors.

TABLE 8.—Five-year corrected survival rates (%), all ages, cases not confirmed by histology

Registries		All stages	Localized		Not localized
England and Wales	1952-53	29.2 ± 3.5*	53.5 ± 8.4	20.3 ± 3.5	
Finland	1953-56	13.6 ± 4.2	25.7 ± 8.8	4.7 ± 3.5	
Norway	1953-56	24.0 ± 4.0	40.6 ± 8.1	12.5 ± 4.2	
U.S. Central	1950-54	24.6 ± 4.0	43.1 ± 10.8	13.0 ± 4.0	
Connecticut	1950-54	26.6 ± 6.2	40.2 ± 16.0	14.2 ± 6.6	
U.S. Hospital	1950-54	38.2 ± 8.3	54.1 ± 16.6	17.6 ± 9.5	
France	1945-57	—	—	—	

\*Two standard errors.

In the U.S. Central registry surgery was followed by a 5-year corrected survival in localized cases of 67 percent in the younger and 60 percent in the older patients. Both these figures were above those found in the European registries where the corresponding results ranged from 41 percent in France for both age groups combined to results in Norway almost comparable with those of the U.S. Central registry. In the more advanced cases there were few contrasts apart from a 5-year corrected survival of 5 percent in the Finnish registry for patients under 70 years compared with 25 percent or more elsewhere (table 9).

Comparison of the corrected survival in the first year after surgery with that in the subsequent 4 years in different registries shows that the greater

TABLE 9.—Five-year corrected survival rates (%) after surgery, in separate age groups and stages

Registries	Age group	Localized		Not localized	
		1945-49	1950-56	1945-49	1950-56
England and Wales	0-69	68.3 ± 11.0	61.7 ± 7.6	25.7 ± 8.4	26.8 ± 7.7
	70-98	40.2 ± 11.6	47.5 ± 7.9	13.1 ± 6.7	22.1 ± 7.1
Finland	0-69	No figures available	45.8 ± 13.4	No figures available	5.3 ± 10.3
	70-98		45.4 ± 17.5		21.6 ± 23.5
Norway	0-69		64.2 ± 7.7		38.1 ± 20.8
	70-98		51.0 ± 7.3		24.8 ± 14.9
U.S. Central	0-69	54.4 ± 6.1	66.9 ± 5.2	26.2 ± 6.9	29.5 ± 6.7
	70-98	53.7 ± 6.4	59.7 ± 6.2	33.5 ± 7.6	30.5 ± 6.6
Connecticut	0-69	51.5 ± 9.4	71.8 ± 7.4	30.6 ± 10.8	28.9 ± 9.4
	70-98	51.5 ± 8.8	54.4 ± 8.5	30.2 ± 10.5	24.5 ± 8.2
U.S. Hospital	0-69	71.1 ± 18.0	73.5 ± 12.9	24.5 ± 17.8	24.5 ± 14.5
	70-98	59.9 ± 22.3	61.3 ± 17.9	29.3 ± 26.5	36.8 ± 20.6
*France (1945-57)	0-69	48.8 ± 32.6 35.5 ± 23.2		26.7 ± 23.8	
	70+				

\*Figures shown for not localized cases of the French registry are for all ages.

TABLE 10.—Comparison of corrected survival rates (%) after surgery in first 12 months with that in the subsequent 48 months for all ages and all degrees of spread

Registries	Corrected survival rate for first 12 months (%)	Corrected survival rate for 13th–60th month (%)
England and Wales	73	57
Finland	66	57
Norway	83	64
U.S. Central	85	61
Connecticut	85	58
U.S. Hospital	82	64
France	63	55

mortality for this condition in the French and the Finnish figures is largely confined to the first 12 months (table 10).

In France the results are affected by limitation of their registration to anticancer centers, where the patients tend to have a poorer prognosis, and where "latent prostatic carcinoma" is unlikely to be treated. A further factor is the period of collection of the French data. In many of the earlier cases, the patients presumably were not given hormones.

### Radiation

Radiation therapy was used in 98 patients with advanced carcinoma of the prostate in the England and Wales registry and in 92 of the French registry patients with not localized disease. Survival was poorer than that in all treatments combined, but selection was undoubtedly a factor. Too few early patients had this form of treatment to draw any useful conclusions.

### Surgery and Radiation

Surgery followed by radiation was also employed infrequently. Among the patients with localized disease in the Finnish registry, 48 had this form of therapy with a 5-year corrected survival of 41 percent. This was poorer than their results in surgery without radiation (46%), but selection again may have affected this.

### Chemical and Hormonal Therapy

Chemical or hormonal therapy includes such diverse procedures as estrogen administration, castration or hypophysectomy, as well as the occasional use of chemicals such as pteroyltriglutamic acid. This group

TABLE 11.—Five-year corrected survival rates (%) after chemical or hormone therapy in separate age groups, 1945-49 and 1950-56, confirmed and not confirmed cases

Registries	Age group	Localized		Not localized	
		1945-49	1950-56	1945-49	1950-56
England and Wales	0-69	66.0 ± 14.6	73.9 ± 12.4	24.7 ± 7.1	28.3 ± 6.5
	70-98	44.7 ± 20.2	42.0 ± 13.2	20.8 ± 8.7	21.2 ± 6.6
Finland	0-69	No figures available	30.4 ± 16.0	No figures available	4.0 ± 5.6
	70-98		22.9 ± 15.2		6.6 ± 9.1
Norway	0-69		53.4 ± 13.9		17.1 ± 7.6
	70-98		44.7 ± 11.1		15.0 ± 6.2
U.S. Central Connecticut	0-69	42.4 ± 16.3	56.3 ± 17.8	13.8 ± 7.2	16.7 ± 7.5
	70-98	50.8 ± 20.6	54.4 ± 17.1	17.4 ± 8.2	14.9 ± 6.5
U.S. Hospital	0-69	33.3 ± 32.8	50.3 ± 30.2	22.6 ± 23.5	18.5 ± 19.2
	70-98	27.0 ± 34.4	45.4 ± 32.7	13.7 ± 18.5	27.6 ± 20.3
France (1945-57)	0-69	63.7 ± 20.5	56.2 ± 18.7	15.0 ± 9.9	21.0 ± 11.5
	70-98	39.6 ± 24.6	47.4 ± 21.8	23.9 ± 16.6	6.3 ± 8.8

of treatments, largely endocrinal, was followed by poorer results than surgery in the United States and Norway registries where the 5-year corrected survival after chemotherapy or hormone treatment in localized disease was 53 to 56 percent in patients under 70 years of age and 45 to 54 percent in the older men.

In England and Wales the corresponding results in early neoplasms for this form of treatment were as high as 74 percent for 63 patients in the younger age group, but only 42 percent in those above 70 years of age, this difference being statistically significant ( $P < 0.01$ ).

In the Finnish figures, the 5-year corrected survival for localized growths after chemotherapy or hormones was 30 percent and 23 percent below and above the age of 70 years, respectively. Contrasts between both these results and those of the U.S. Central or Norway registry were statistically significant ( $P < 0.05$ ) (table 11).

In the limited-stage breakdown used, it is difficult to compare the effects of different treatments in advanced neoplasms. For treatment by chemotherapeutic or hormonal drugs, the corrected 5-year survival of patients with not localized cancer was about 18 to 20 percent, and somewhat higher than in patients with advanced prostatic cancer given radiation therapy where the corresponding figure was 7 to 10 percent.

Examination of the corrected survival in the first 12 months after chemotherapy or hormone therapy, and again in the subsequent 4 years, reveals that with this form of treatment the comparatively poor results in Finland occur in both these periods; in fact, the contrast with other registries is more noticeable in the last 4 years.



TRENDS IN TWO PERIODS SHOWN IN ENGLAND AND WALES  
AND THE UNITED STATES

In comparing the results in the period preceding 1950 with the later figures, we found an improvement in the survival of localized cases in the U.S. Central registry after surgery and chemical or hormonal therapy to the extent of 9 percent in both these forms of treatment in the 5-year corrected survival of all ages combined. This improvement is statistically significant in the results following surgery ( $P < 0.01$ ).

In England and Wales, on the other hand, the improvement after 1950 is confined to the advanced cases, more especially following operative treatment of the cancer.

## SUMMARY

Some contrasts are discussed in data relating to prostatic malignancy collected by cancer registries of France, the United States, Finland, Norway, and England and Wales, with particular reference to end results of treatment.

In Norway, where the mortality due to this condition is the highest of the five participant countries, the proportion of older patients is greater than elsewhere.

Surgery was more commonly used than any other form of treatment, particularly in the U.S. Central registry, where a preference for surgery was shown even in cases not described as localized.

In Finland, Norway, and the England and Wales registries, hormonal therapy or chemotherapy was employed in roughly one fourth of the localized cases and 40 to 60 percent of the more advanced.

The 5-year corrected survival for all cases was 38 percent, the results being markedly affected by the degree of spread of the growth on treatment. In spite of correction for age, the survival was also poorer in older patients with localized disease.

The differences between the survival rates of each country are discussed.

### **Summary of General Discussion**

Possible explanations of the unusually low survival rates for the disease in Finland were discussed. It was pointed out that the low survival rates found in Finland might be an artifact of diagnostic criteria and classification.

It was suggested that it would be of interest to see whether correspondingly low survival rates would be found in other countries with low incidence of the disease, as, for instance, Japan. However, in cancer of the breast, a low incidence in Japan is associated with a high survival rate.

## **Cancer of the Testis**

Survival of Patients With Malignant Tumors of the Testis. KNUT MAGNUS,  
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### GENERAL DISCUSSION

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## Survival of Patients With Malignant Tumors of the Testis

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TEN series of data on malignant tumors of the testis have been collected from six sources: England and Wales, Finland, Norway, U.S. Central registries, including Connecticut, and U.S. Teaching Hospitals. The data from England and Wales and the United States are given for two periods.

### INCIDENCE

An evaluation of the incidence of the disease cannot be given from the material presented here. Cases first diagnosed at autopsy and those based on death certificates only have been excluded. Furthermore, for some of the series estimates of "the population at risk" are not available. Attention is drawn however to the difference in the number of cases reported from Finland and Norway (table 1). Although the population of Finland is slightly larger than that of Norway, only 67 cases are reported from Finland as compared to 216 cases from Norway.

A comparison of incidence rates of malignant tumors of the testis based on total registry material in the two countries (1, 2) with those of Connecticut (3), Denmark (4), and Sweden (5) discloses marked variations. Whereas in the Finnish population the annual rate per 100,000 is less than 1, the rate varies between 2.5 and 4.0 in the other populations. These data leave no doubt as to the statistical significance of this difference.

### HISTOLOGY

The material comprises a total of 1,571 cases of which 1,471 were confirmed histologically. The following analysis is based on the confirmed cases only.

The histologically confirmed malignant tumors have been grouped as seminomas or "other or unspecified histological type." Marked

TABLE 1.—Number of cases of malignant tumors of the testis

Country and year of diagnosis		Histologically confirmed	Not histologically confirmed	Total
Finland	1953-56	63	4	67
Norway	53-56	212	4	216
England and Wales	48-49	251	49	300
England and Wales	52-53	364	22	386
U.S. Central registry	45-49	210	11	221
U.S. Central registry	50-54	213	7	220
Connecticut	45-49	107	5	112
Connecticut	50-54	116	3	119
U.S. Teaching Hospitals	45-49	74	1	75
U.S. Teaching Hospitals	50-54	84	2	86
Total*		1,471	100	1,571

\*The figures from Connecticut are included in the figures from U.S. Central registries.

variations are found in the distributions by histological type. The proportion of seminomas ranges from 27 to 67 percent (table 2).

The proportion of tumors classified as seminomas was higher in the European series than in those of the United States. It does not seem justified, however, to conclude from this observation that there are real differences in the distributions by histological type. Variations in the pathological classification of the testis tumors may well be responsible. This assumption is supported by the fact that in the three sets of data from the United States there was a shift toward a higher proportion of seminomas from the first to the second period.

### AGE DISTRIBUTION

The material has been divided into three age groups: less than 35 years, 35 to 44 years, and 45 years or older. The age distribution of the materials is rather similar: 40 to 50 percent, less than 35 years; 25 to 35 percent, between 35 and 45 years; and 20 to 30 percent, more than 45 years (table 3). The number of cases reported from Finland

TABLE 2.—Malignant tumors of the testis by histological type

Country and year of diagnosis		Number of histologically confirmed cases	Seminoma (%)	Other or unspecified (%)
Finland	1953-56	63	55.6	44.4
Norway	53-56	212	60.3	39.7
England and Wales	48-49	251	66.9	33.1
England and Wales	52-53	364	57.1	42.9
U.S. Central registry	45-49	210	29.5	70.5
U.S. Central registry	50-54	213	42.2	57.8
Connecticut	45-49	107	36.4	63.6
Connecticut	50-54	116	52.6	47.4
U.S. Teaching Hospitals	45-49	74	27.0	73.0
U.S. Teaching Hospitals	50-54	84	39.3	60.7

TABLE 3.—Histologically confirmed cases of malignant tumors of the testis by age

Country and year of diagnosis	Percentage distribution by age								
	All confirmed cases			Seminoma			Other and unspecified type		
	<34	35-44	45 and over	<34	35-44	45 and over	<34	35-44	45 and over
Finland 1953-56	33.3	25.4	41.3	25.7	28.6	45.7	42.9	21.4	35.7
Norway 53-56	47.6	29.7	22.7	39.1	34.3	26.6	60.7	32.6	16.7
England and Wales 48-49	37.0	34.3	28.7	29.2	39.3	31.5	53.0	24.1	22.9
England and Wales 52-53	40.1	31.6	28.3	29.3	37.5	33.2	54.5	23.7	21.8
U.S. Central registry 45-49	47.6	24.8	27.6	33.9	19.4	46.7	53.4	27.0	19.6
U.S. Central registry 50-54	49.3	28.2	22.5	42.2	27.8	30.0	54.5	28.5	17.0
Connecticut 45-49	47.7	24.3	28.0	41.0	15.4	43.6	51.5	29.4	19.1
Connecticut 50-54	47.4	31.0	21.6	44.2	27.9	27.9	50.9	34.5	14.6
U.S. Teaching Hospitals 45-49	51.4	27.0	21.6	35.0	35.0	30.0	57.4	24.1	18.5
U.S. Teaching Hospitals 50-54	50.0	31.0	19.0	45.5	33.3	21.2	52.9	29.4	17.7





is small and the observed deviation from this distribution is not significant. The patients with seminoma differ in age from those of "other or unspecified type." More than one half of the latter group and only about one third of the seminoma patients are less than 35 years old.

### STAGE DISTRIBUTION

The proportion of cases classified as localized varies between 50 and 68 percent (table 4). As will be discussed later, these differences are more likely to be due to variations in diagnostic technique and classification than to real differences in the stage distribution of the patients.

### TREATMENT

Surgery alone or surgery combined with radiotherapy was given to more than 90 percent of the patients in all the series (table 5). The combined treatment was more frequently used in England and Wales and Norway than in the other countries. About 80 percent of the patients received this treatment in England and Wales and Norway as compared to 50 to 70 percent in Finland and the United States.

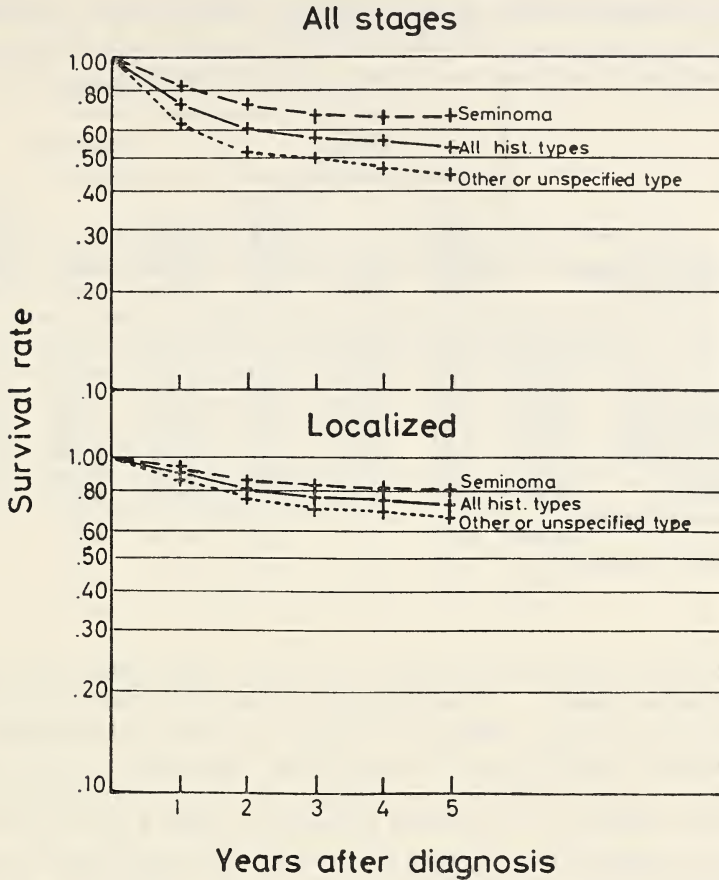
The relative frequency of the two main types of treatment, surgery alone and surgery-radiotherapy combined, was stable from the first to the second period in the sets of data from England and Wales and the United States. In the material from Europe, surgery alone was less frequently given to the seminoma patients than to those of "other or unspecified type." In the United States this difference in treatment of the two groups of patients was observed for the most recent period only. Whether this reflects a real change in the selection of patients for the two types of treatment or simply the shift in pathological classification mentioned cannot be determined from these data.

### SURVIVAL

Five years after diagnosis, 56 of the total 1,471 cases were untraced. This proportion lost to follow-up (3.8%) is significantly higher than that observed, for example, in the material for cancer of the stomach (6). If the registration of deaths is relatively complete, this variation is not surprising with the difference in survival from cancer of the two sites taken into account.

TABLE 5.—Histologically confirmed cases of malignant tumors of the testis by primary treatment

Country and year of diagnosis	Percentage distribution by primary treatment					
	All confirmed cases		Seminoma		Other and unspecified type	
	Surgery	Surgery + radiation	Other or no treatment	Surgery	Surgery + radiation	Other or no treatment
Finland 1953-56	39.7	54.0	6.3	31.4	50.0	7.1
Norway 53-56	17.5	79.7	2.8	9.4	29.8	3.6
England and Wales 48-49	13.5	80.5	6.0	11.3	18.1	8.4
England and Wales 52-53	14.3	77.2	8.5	10.1	19.9	7.0
U.S. Central registry 45-49	42.9	47.6	9.5	35.5	45.9	10.2
U.S. Central registry 50-54	44.6	49.3	6.1	24.4	59.3	9.0
Connecticut 45-49	29.9	63.6	6.5	30.8	29.4	7.3
Connecticut 50-54	36.2	61.2	2.6	19.7	54.5	3.7
U.S. Teaching Hospitals 45-49	33.8	60.8	5.4	40.0	31.5	5.5
U.S. Teaching Hospitals 50-54	26.1	70.2	3.7	18.2	31.4	1.9



TEXT-FIGURE 1.—Histologically confirmed cases of malignant tumors of the testis. Corrected survival rates up to 5 years after diagnosis; all materials combined; unweighted average.

The corrected survival rates shown in text-figure 1 represent unweighted averages of the rates from all series to demonstrate the trend in mortality up to 5 years after diagnosis. Mortality is high during the first years with more than four-fifths of all deaths occurring within 2 years after diagnosis. Between 2 and 5 years after diagnosis there is, however, also a deviation from the "normal" survival experience, although the excess mortality is very slight for the seminoma group.

The average 5-year corrected survival rate was 0.54 for all cases of malignant tumor of the testis. There is a marked difference in survival between the two main histological groups, the rates being 0.66 for the seminomas and 0.44 for "other or unspecified types."

TABLE 6.—Five-year survival rate of histologically confirmed cases of malignant tumors of the testis

Country and year of diagnosis		Five-year corrected survival rate					
		All stages			Localized		
		All histological types	Seminoma	Other and unspecified type	All histological types	Seminoma	Other and unspecified type
Finland	1953-56	0.54	0.59	0.48	0.70	0.77	0.61
Norway	53-56	0.55	0.66	0.38	0.73	0.78	0.63
England and Wales	48-49	0.54	0.57	0.48	0.71	0.71	0.71
England and Wales	52-53	0.62	0.69	0.52	0.79	0.84	0.72
U.S. Central registry	45-49	0.48	0.66	0.40	0.61	0.82	0.52
U.S. Central registry	50-54	0.53	0.75	0.37	0.75	0.82	0.67
Connecticut	45-49	0.48	0.71	0.35	0.57	0.80	0.43
Connecticut	50-54	0.54	0.79	0.26	0.73	0.81	0.56
U.S. Teaching Hospitals	45-49	0.52	0.72	0.45	0.72	0.81	0.67
U.S. Teaching Hospitals	50-54	0.55	0.69	0.46	0.81	0.87	0.74

The 5-year corrected survival rate for all cases ranges from 0.48 to 0.62 in the 10 series (table 6). Considering the rather small numbers involved, the results are uniform. Nine of the 10 rates vary between 0.48 and 0.55.

A consistent classification of the material by histological type and stage would form a good basis for an evaluation of the effect of treatment in the various countries. The results presented in table 6 for the various subgroups suggest, however, that this aim of the classification has not been achieved. The variability in results for the subgroups is greater than for the total groups of the series. The 5-year survival rate ranges from 0.57 to 0.79 for the seminoma groups, from 0.26 to 0.52 for the "other or unspecified type" group, and from 0.57 to 0.81 for the group of localized cases of all histological types. The lack of uniformity in the classification by stage is also indicated by the missing correlation between the proportion of cases classified as localized (table 4) and the survival rate of the cases of all stages combined.

No conclusions can therefore be drawn as to differences in the effect of treatment in the various countries. Interestingly, however, the survival rates were consistently higher for the second than for the first period in the series from England and Wales and the United States. Although one cannot exclude a difference in selection of patients during the two periods, this might indicate an improvement in the effect of treatment.

As previously mentioned, there was no difference in the frequency of the two main types of treatment for the two periods. The improvement in prognosis suggested by the data might possibly have been caused by a



development of diagnostic criteria enabling a more rational choice from among available methods of treatment, by improvements in the surgical or radiological technique, or by more efficient secondary treatment.

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### **Summary of General Discussion**

The pathologists agreed that the histological grouping was not satisfactory, and there was considerable discussion regarding classification. It was concluded that, even if a more detailed classification were used in future studies, the classification would have to be tested and standardized through "blind" examination of histological specimens.

The increased survival of patients from the first to the second period, shown in the basic material, might be due to improvements in treatment. At the Norwegian Radium Hospital, the patient material was divided in two groups according to the skin dose the patients had received at each treatment field. The group receiving the higher doses had a much better survival rate. Since 1950 (the same year the second period in the series from England and Wales and the United States started) use of supervoltage treatment has increased.

## Melanoma of the Skin

Survival Rates for Melanomas of the Skin. KNUD LOCKWOOD, BENT STANCKE,  
and JOHANNES CLEMMESSEN, Denmark

### GENERAL DISCUSSION

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Presented at the International Symposium on End Results of Cancer Therapy,  
Sandefjord, Norway, September 16-20, 1963.





## Survival Rates for Melanomas of the Skin<sup>1</sup>

KNUD LOCKWOOD, *D.M.Sc.*, BENT STANCKE, *B.P.Sc.*, and JOHANNES CLEMMESEN, *D.M.Sc.*,<sup>2</sup> *Danish Cancer Registry Under the National Anti-Cancer League, Copenhagen, Denmark*

A full evaluation of results for this and other contributions to this volume, as well as of their limitations in applicability to comparisons, requires careful study of the composition of the data collected for the site in question in the setting of the national data. Without the assistance of the organizations collecting the material, it is dangerous to draw conclusions except on a very gross scale.

An example of what might be achieved in the study of melanomas is the recent monograph of Jensen (1) on malignant melanomas of the uvea in Denmark. This monograph gives a full analysis of all cases occurring in an entire country within a limited period, both from clinical-histological and from statistical points of view. In the present connection, Jensen's study is of interest with regard to its estimate of survival rates for different sex and age, and for various cell types, as well as in relation to content of pigment and reticulin.

At the moment such an estimate is not possible for cutaneous melanomas because of less centralized treatment of these tumors, but it may become possible in the future.

The data included under the present analysis are the following: 1) "United States" figures from data from the centralized cancer registries in Connecticut, California, and Massachusetts and a number of teaching hospitals in the United States; 2) data from the Norwegian Cancer Registry; 3) data from the Finnish Cancer Registry; 4) data

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<sup>2</sup> The authors are grateful to Miss Marie Lindhardt, D.M.h.c., B.P.Sc., for statistical advice.

from the Danish Cancer Registry; 5) data from France pertaining only to patients seen in 22 cancer centers that generally specialize in radiotherapy; and 6) data from Great Britain. The presentation is restricted to cases with microscopically confirmed diagnoses.

The data are summarized in text-figures 1 through 6. More detailed data are contained in tables 1 through 6.

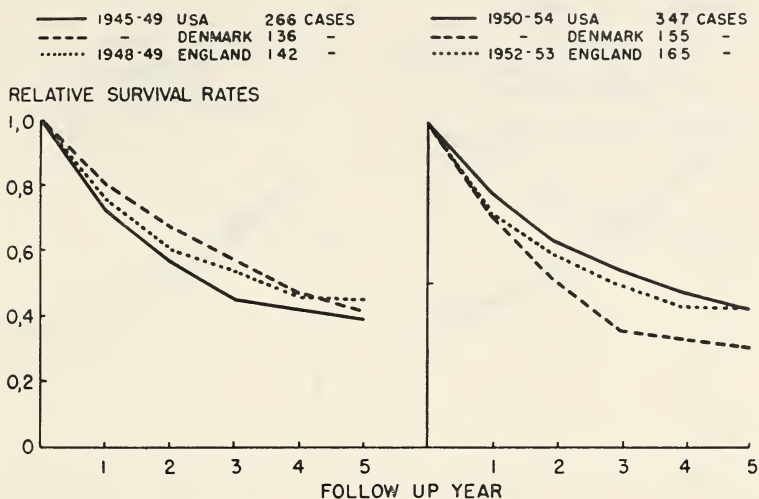
Comparing the survival results presented with survival studies by other authors, one may be surprised by the high relative survival rate demonstrated in this material. White (2) reviews 5-year survival statistics on cutaneous melanoma by several authors [Catlin (3), Preston *et al.* (4), Lund and Ihnen (5), Brandt (6), and Vogler *et al.* (7)]. Five-year survival reaches from 21 to 25 percent among males and from 20 to 33 percent among female patients. A personal communication with Dr. Grete Olsen (8) from the Finsen Institute in Copenhagen reveals a 5-year survival of 22 percent among males and 57 percent among females. Although one cannot directly compare relative survival rates to 5-year survival percentages, clearly there is a difference among the material presented here and survival percentages found by other authors. However, our material is from cancer registries, in contrast with the material compiled by other authors who present determinate selected cases mostly treated in their clinics.

It is therefore emphasized that our data be handled with great care before any conclusions are drawn. The reason why 6 international registries present a definitely minor mortality compared to materials selected by surgical clinics is probably that cancer registries get notification on patients who have been surgically treated for a cutaneous lesion which in most cases could be a malignant melanoma. The pathologist concerned may prefer to overdiagnose a lesion as a melanoma knowing that such a diagnosis will assure surgical treatment for the patient. It is clear that this tends to improve our relative survival rates. In accordance with other authors, the present material demonstrates a higher survival rate for female than for male patients.

MELANOMA IN USA, DENMARK AND ENGLAND.

MALES ALL AGES.

TOTAL TREATED AND UNTREATED CASES. ALL STAGES

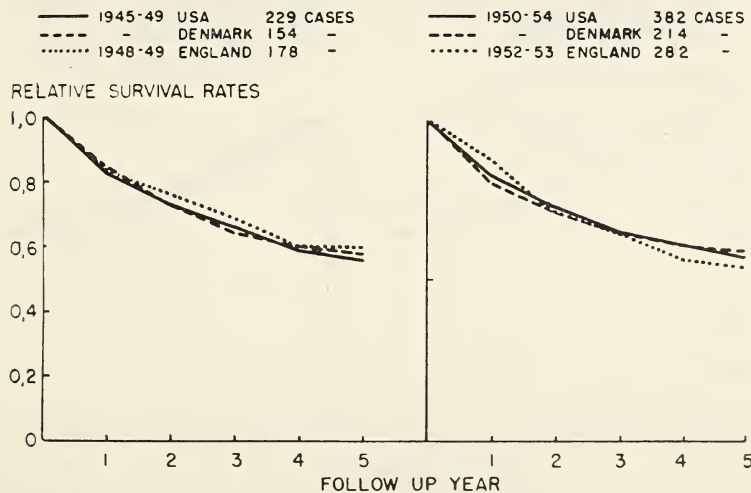


TEXT-FIGURE 1.—Melanoma cases for the United States, Denmark, and England, treated and untreated, show a relative survival after 5 years of about 50 per cent for men.

MELANOMA IN USA, DENMARK, ENGLAND.

FEMALES ALL AGES

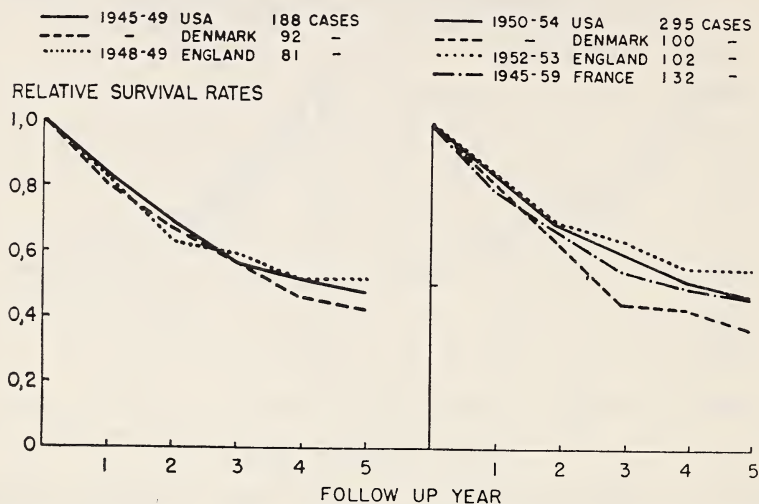
TOTAL TREATED AND UNTREATED CASES. ALL STAGES.



TEXT-FIGURE 2.—The curves for all cases, treated and untreated, for women, show considerably better survival than for men, in all countries, for both periods.

MELANOMA IN USA, DENMARK, ENGLAND - FRANCE.  
SURGERY ALL STAGES

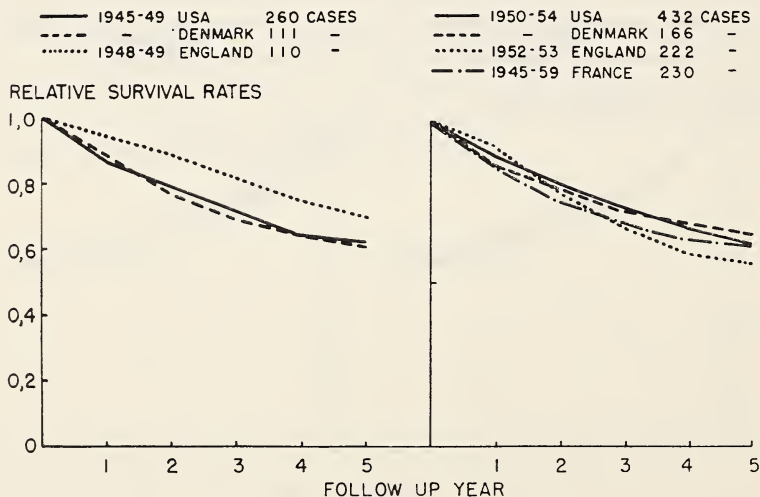
MALES ALL AGES



TEXT-FIGURE 3.—All cases treated with surgery, irrespective of stage, show only slight improvement (cf. text-fig. 1).

MELANOMA IN USA, DENMARK, ENGLAND - FRANCE.  
SURGERY ALL STAGES.

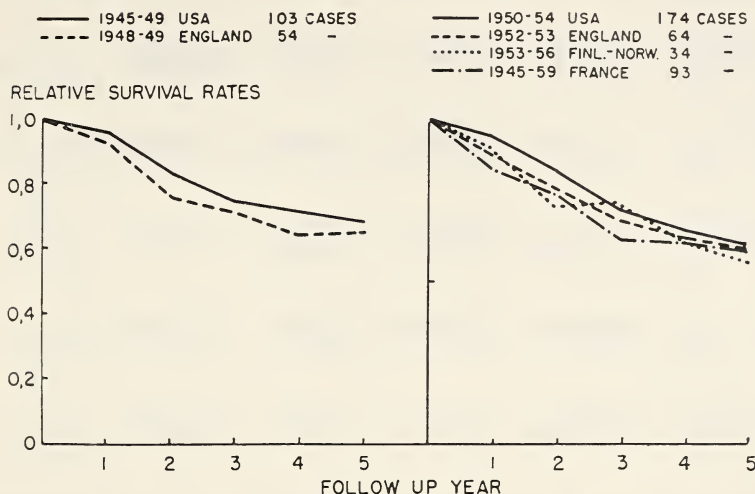
FEMALES ALL AGES.



TEXT-FIGURE 4.—Surgery for all stages shows no essential improvement for women.

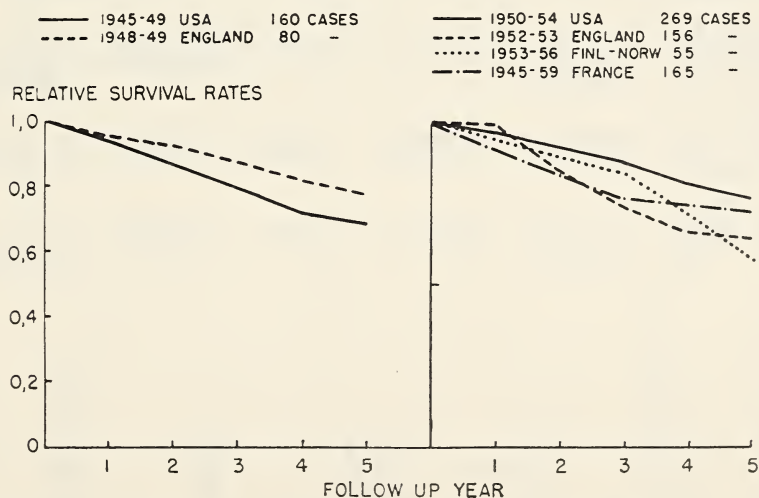


MELANOMA IN USA, ENGLAND - FRANCE, FINL.-NORWAY. MALES ALL AGES.  
SURGERY LOCALIZED.



TEXT-FIGURE 5.—When the survey is restricted to cases known to have been localized—with Denmark omitted—the survival is considerably better. These cases treated under favorable conditions amount to about one third of all cases in England and the United States, for men.

MELANOMA IN USA, ENGLAND - FRANCE, FINL.-NORWAY. FEMALES ALL AGES.  
SURGERY LOCALIZED.



TEXT-FIGURE 6.—Surgery for localized cases shows the best results on record. The fraction of women treated with surgery is far larger for all countries and for both periods.

TABLE 1.—Melanoma, all ages and stages (males)—United States, Denmark, and England

	United States						Denmark						England					
	1945-49			1950-54			1945-49			1950-54			1948-49			1952-53		
	Cases	Rates		Cases	Rates		Cases	Rates		Cases	Rates		Cases	Rates		Cases	Rates	
Surgery																		
0-1 year(s)	188	0.84		295	0.84		92	0.80		100	0.82		81	0.82		102	0.85	
1-2 "	150	.71		236	.69		72	.67		80	.63		62	.63		83	.69	
2-3 "	121	.59		184	.61		59	.56		45	.45		45	.59		65	.64	
3-4 "	96	.54		157	.52		48	.46		41	.43		40	.52		57	.56	
4-5 "	83	.49		126	.47		39	.42		38	.37		33	.52		48	.55	
Radiation																		
0-1 year(s)	16	.56		7	.29		24	.79		24	.57		16	.59		19	.27	
1-2 "	9	.20		2	.15		18	.65		13	.27		8	.48		5	.28	
2-3 "	3	.14		1	.00		14	.64		6	.19		6	.44		5	.24	
3-4 "	2	.07		—			13	.53		4	.15		5	.30		4	.24	
4-5 "	1	.04		—			10	.45		3	.16		3	.34		4	.26	
Surgery + radiation																		
0-1 year(s)	15	.63		5	.43		2	1.01		2	1.03		41	.77		33	.78	
1-2 "	9	.44		2	.00		2	.52		2	.53		31	.69		24	.54	
2-3 "	6	.32		—			1	.00		1	.00		27	.57		16	.38	
3-4 "	4	.36		—			—			—			22	.48		11	.25	
4-5 "	4	.41		—			—			—			18	.46		6	.25	
No known treatment																		
0-1 year(s)	47	.29		40	.37		18	.85		29	.43		4	.26		11	.09	
1-2 "	13	.14		13	.24		15	.75		12	.29		1	.26		1	.10	
2-3 "	6	.15		8	.20		13	.71		8	.19		1	.27		1	.10	
3-4 "	6	.08		6	.22		12	.55		5	.16		1	.28		1	.11	
4-5 "	3	.05		6	.16		9	.50		4	.16		1	.29		1	.11	
Total treated and untreated																		
0-1 year(s)	266	.71		347	.76		136	.81		155	.72		142	.76		165	.72	
1-2 "	181	.56		253	.61		107	.68		107	.51		102	.61		113	.57	
2-3 "	136	.47		193	.53		87	.58		74	.36		79	.54		87	.50	
3-4 "	108	.42		163	.46		73	.48		50	.33		46	.46		73	.43	
4-5 "	91	.38		132	.41		58	.42		45	.30		55	.46		59	.42	

TABLE 2.—Melanoma, all ages and stages (females)—United States, Denmark, and England

	United States						Denmark						England					
	1945-49			1950-54			1945-49			1950-54			1948-49			1952-53		
	Cases	Rates	Cases	Rates	Cases	Rates	Cases	Rates	Cases	Rates	Cases	Rates	Cases	Rates	Cases	Rates	Cases	Rates
<b>Surgery</b>																		
0-1 year(s)	229	0.86	382	0.87	111	0.88	166	0.86	110	0.94	222	0.92						
1-2 "	189	.77	327	.77	96	.77	140	.79	101	.89	198	.78						
2-3 "	165	.71	281	.71	82	.69	126	.72	94	.82	163	.67						
3-4 "	148	.64	250	.66	72	.64	112	.68	84	.75	136	.59						
4-5 "	127	.61	216	.62	65	.61	105	.65	74	.70	117	.56						
<b>Radiation</b>																		
0-1 year(s)	5	.64	3	.34	21	.73	22	.62	11	.57	14	.66						
1-2 "	3	.00	1	.00	15	.54	13	.40	6	.49	9	.45						
2-3 "	—	—	—	—	11	.40	8	.41	5	.51	6	.46						
3-4 "	—	—	—	—	8	.36	8	.38	5	.53	5	.47						
4-5 "	—	—	—	—	7	.37	7	.34	5	.55	5	.48						
<b>Surgery + radiation</b>																		
0-1 year(s)	10	.51	9	.46	6	.50	3	.33	50	.75	33	.81						
1-2 "	5	.31	4	.47	3	.51	1	.34	37	.64	26	.48						
2-3 "	3	.21	4	.36	3	.34	1	.34	31	.53	15	.43						
3-4 "	2	.21	3	.36	2	.35	1	.34	25	.48	13	.40						
4-5 "	2	.21	3	.36	2	.18	1	.34	22	.40	12	.35						
<b>No known treatment</b>																		
0-1 year(s)	16	.39	38	.21	16	.82	23	.58	7	.15	13	.57						
1-2 "	5	.33	8	.16	13	.83	13	.45	1	.00	7	.42						
2-3 "	4	.35	6	.08	13	.78	10	.42	—	—	5	.27						
3-4 "	4	.37	3	.08	12	.79	9	.38	—	—	3	.09						
4-5 "	4	.30	3	.08	12	.80	8	.39	—	—	1	.10						
<b>Total treated and untreated</b>																		
0-1 year(s)	260	.81	432	.80	154	.84	214	.80	178	.83	282	.88						
1-2 "	202	.71	340	.71	127	.73	167	.71	145	.76	240	.71						
2-3 "	172	.65	291	.65	109	.65	145	.65	130	.69	189	.65						
3-4 "	154	.59	256	.60	94	.60	130	.62	114	.62	157	.57						
4-5 "	133	.57	222	.57	86	.58	121	.59	101	.60	135	.54						

TABLE 3.—Melanoma, all ages and stages, 1953–1956 (males and females)—Finland and Norway

	Males				Females			
	Finland		Norway		Finland		Norway	
	Cases	Rates	Cases	Rates	Cases	Rates	Cases	Rates
Surgery								
0–1 year(s)	21	0.54	48	0.72	29	0.80	48	0.88
1–2 "	11	.35	31	.58	21	.74	41	.76
2–3 "	7	.36	24	.49	19	.71	34	.67
3–4 "	7	.37	20	—	18	.64	29	—
4–5 "	7	.39	11	—	16	—	20	—
Radiation								
0–1 year(s)	9	.70	5	.61	16	.57	4	.53
1–2 "	6	.37	3	.41	9	.45	2	.28
2–3 "	3	.13	2	.41	7	.46	1	.30
3–4 "	1	.14	2	.42	7	.40	1	.32
4–5 "	1	.14	2	.42	6	.32	1	.34
Surgery + radiation								
0–1 year(s)	50	.79	91	.86	91	.92	108	.88
1–2 "	39	.60	77	.72	81	.74	92	.77
2–3 "	28	.54	63	.61	64	.66	80	.69
3–4 "	25	.44	52	—	56	.57	70	—
4–5 "	20	—	37	—	45	—	41	—
No known treatment								
0–1 year(s)	13	.24	8	.25	13	.23	4	.14
1–2 "	3	.24	2	.25	2	.23	—	—
2–3 "	3	.17	2	.13	2	.23	—	—
3–4 "	2	.09	1	.00	2	.23	—	—
4–5 "	1	.09	—	—	2	.23	—	—
Total treated and untreated								
0–1 year(s)	93	.65	152	.78	149	.81	164	.85
1–2 "	59	.47	113	.64	113	.67	135	.74
2–3 "	41	.41	91	.54	92	.62	115	.66
3–4 "	35	.35	75	—	83	.54	100	—
4–5 "	29	—	50	—	69	—	62	—



TABLE 4.—Melanoma, all ages; surgery, localized and not localized (males and females)—United States, England, Finland, and Norway

	United States				England				Finland and Norway	
	1945-49		1950-54		1948-49		1952-53		1953-56	
	Cases	Rates	Cases	Rates	Cases	Rates	Cases	Rates	Cases	Rates
<b>Males</b>										
Surgery										
localized										
0-1 year(s)	103	0.97	174	0.94	54	0.93	64	0.89	34	0.91
1-2 "	96	.87	156	.84	48	.76	54	.79	29	.73
2-3 "	82	.80	131	.75	37	.71	47	.69	23	.74
3-4 "	71	.77	113	.68	33	.64	40	.64	23	.62
4-5 "	64	.73	97	.64	28	.65	36	.60	16	.56
Surgery not										
localized										
0-1 year(s)	73	.61	98	.63	27	.57	38	.80	27	.38
1-2 "	43	.44	60	.41	14	.34	29	.52	10	.24
2-3 "	30	.24	38	.36	8	.31	18	.52	6	.12
3-4 "	18	.21	32	.22	7	.23	17	.39	3	.08
4-5 "	13	.17	18	.16	5	.24	12	.41	1	.00
<b>Females</b>										
Surgery										
localized										
0-1 year(s)	160	.94	269	.97	80	.96	156	.99	55	.94
1-2 "	145	.87	250	.93	75	.93	149	.85	49	.89
2-3 "	131	.83	228	.89	71	.88	126	.74	45	.84
3-4 "	120	.75	210	.83	66	.82	106	.66	41	.72
4-5 "	103	.73	181	.78	60	.78	93	.64	31	.58
Surgery not										
localized										
0-1 year(s)	54	.59	93	.64	30	.89	66	.76	18	.62
1-2 "	31	.49	58	.42	26	.81	49	.59	11	.41
2-3 "	25	.42	38	.33	23	.65	37	.49	7	.29
3-4 "	21	.37	28	.29	18	.56	30	.41	5	.23
4-5 "	18	.35	24	.30	14	.49	24	.37	4	.17

TABLE 5.—Melanomas, all ages, 1945-1959; surgery, localized and not localized (males and females)—France

	Males		Females	
	Cases	Rates	Cases	Rates
Surgery localized				
0-1 year(s)	93	0.85	165	0.92
1-2 "	70	.77	138	.84
2-3 "	59	.63	115	.77
3-4 "	36	.62	88	.75
4-5 "	28	.60	64	.73
Surgery not localized				
0-1 year(s)	35	.74	54	.69
1-2 "	25	.48	36	.54
2-3 "	14	.41	26	.41
3-4 "	10	.25	15	.34
4-5 "	5	.21	12	.32
Total				
0-1 year(s)	128	.80	219	.86
1-2 "	95	.67	174	.76
2-3 "	73	.55	141	.68
3-4 "	46	.50	103	.64
4-5 "	33	.47	76	.62

TABLE 6.—Melanomas, all ages, 1945-1959; surgery + radiation, localized and not localized (males and females)—France

	Males		Females	
	Cases	Rates	Cases	Rates
Surgery + radiation, localized				
0-1 year(s)	133	0.85	228	0.89
1-2 "	97	.75	179	.80
2-3 "	78	.61	142	.74
3-4 "	51	.56	112	.71
4-5 "	38	.54	78	.68
Surgery + radiation, not localized				
0-1 year(s)	96	.47	107	.58
1-2 "	41	.32	58	.41
2-3 "	25	.26	36	.29
3-4 "	15	.17	19	.25
4-5 "	8	.13	15	.22
Total				
0-1 year(s)	229	.68	335	.79
1-2 "	138	.56	237	.67
2-3 "	103	.45	178	.60
3-4 "	66	.39	131	.56
4-5 "	46	.36	93	.53

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### Summary of General Discussion

Attention was called to the sex differential in incidence as well as in survival rates. Women have consistently higher incidence rates and higher survival rates than men, as in several other forms of cancer. For malignant melanomas of the skin, the sex difference in prognosis is observed only in cases classified as localized and only in younger women. Furthermore, observations were reported indicating that the excess incidence as well as the more favorable prognosis is mainly confined to certain anatomical sites, notably the legs.

It was suggested that the observed phenomenon may result from a greater tendency to include women in whom melanomas are not in fact frankly malignant. This could easily occur if moles are much more frequently removed (*e.g.*, for cosmetic reasons) in women than in men. The pathologists were not convinced that more moles are excised and submitted for histopathological examination from females than from males, and they did not think that the distinction between benign and malignant moles was more difficult in females. However, moles removed during pregnancy do present a problem. They agreed that the problem deserved further study.

The merits of various more or less extensive surgical procedures in treatment of malignant melanoma of the skin were briefly discussed.



## **Cancer of the Tongue**

Survival Experience of Patients From Five Countries With Cancer of the Tongue, Around 1950–1954. H. CAMPBELL, Wales

Malignant Tumors of the Tongue Treated at the Norwegian Radium Hospital, 1932–1958. ERIK POPPE, Norway

### **GENERAL DISCUSSION**

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Presented at the International Symposium on End Results of Cancer Therapy, Sandefjord, Norway, September 16–20, 1963.



## **Survival Experience of Patients From Five Countries With Cancer of the Tongue, Around 1950-1954**

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PHYSICIANS long believed that the tongue was a mirror of the general state of health, largely because this was the only part of the alimentary canal that was easily accessible for examination. Modern techniques for examining the interior of the gastrointestinal tract should not blind us to the necessity for inspection and palpation of the tongue itself when making a general examination of a patient to detect early neoplastic changes.

The lymphatics of the tongue drain into the various cervical nodes, according to the region of the tongue involved, which are all easy to palpate and may be biopsied easily. In consequence, it should be possible to detect all neoplasms of the tongue at a very early stage and to reduce the mortality considerably. Unfortunately, this is not always successful, and patients still delay seeking medical advice until the disease has spread to regional nodes.

### **THE REGISTERS**

In the present study of survival experience from cancer of the tongue, 7 registers were included in the analysis. The Connecticut cancer register covered all cases of cancer known to occur in that state, and the results of these cases are reported twice, first by themselves as a complete register of all cases arising in a defined population, and secondly as part of the U.S. Central registers which covered the States of California, Connecticut, and Massachusetts; the patients on the California and Massachusetts registers were not a complete sample of all cases within these two states at this period of time. The U.S. Hospitals register includes a number of

large teaching hospitals and major regional centers; it thus represents a sample of some of the best results to be expected from a hospital population. The England and Wales register consists of an amalgam of a complete population register for approximately one third of the country and cases from a sample of the larger hospitals and radiotherapy centers in the rest of the country. The French register consists of all patients referred to the anticancer therapy centers throughout the country.

The registers from Finland and Norway include all patients from 1953 on.

The number of cases from England, Finland, Norway, and the United States included in this study of cancer of the tongue around the period 1950-54 was 2,450-1,811 males and 639 females. The number of cases included in the French register alone was 4,735-4,155 males and 580 females.

### SEX DISTRIBUTION

There was wide variation in the sex ratio among the cases registered with the Ad Hoc Group. In Norway and Finland, neoplasm of the tongue was almost as frequent in women as in men, whereas the ratio in England was 3 men to 1 woman, in the United States 4 to 1, and in France 7 to 1 (table 1).

TABLE 1.—Female cases per 100 males

England	38
Finland	92
France	14
Norway	93
United States (Calif., Conn., Mass.)	25
United States (Conn.)	27
United States (Hospitals)	22

The End Result study was not designed to study the possible etiological or epidemiological significance of these ratios, but independent consideration of the published rates of incidence of new cases and national mortality confirm that this is the general pattern of the disease.

Table 2 shows that there was not a great difference between the various countries in the female rates for new cases, but that there was a marked difference between the rate for males in England and Connecticut as compared with Norway and Finland. This strongly suggests that there is a particular etiological agent present in the former two countries.

Important though these differences may be in a study of etiology, it is unlikely that they would have a serious effect on the results of this study of survival rates as the sexes have been kept distinct throughout the study in this paper.



TABLE 2.—Rates per million population for new cases of cancer of the tongue and for deaths, by sex

Country or register		New cases		Mortality	
		Male	Female	Male	Female
England and Wales	1954-58	—	—	17	7
Southwest England	1954-58	26	11	—	—
Connecticut	1947-51	36	7	19	3
Norway	1953-58	10	7	7	5
Finland	1953-56	7	6	4	4

## AGE DISTRIBUTION

The only age division used in these tabulations was a dichotomy between patients over and under 65 years of age. This division split the cases into two almost equal groups, except for those on the English register where it is apparent that the average age of English patients must have been higher than in the other countries and in France where the patients must have been younger (table 3).

## STAGE OF THE DISEASE

In the prognosis of cancer of the tongue, the single most important factor is the stage at which the disease is first diagnosed, and it is important to note that in all registers women were diagnosed at an earlier stage than men (table 4).

Frequently there is difficulty in agreement among various countries on the staging of a disease, but in neoplasm of the tongue, where the boundaries of the organ are well defined, the only difficult cases are likely to be fungating carcinomas of the floor of the mouth or a few hypopharyngeal cancers which should be relatively rare. These great differences in the severity of the disease in various countries may be attributed to: 1) a difference in the disease itself and its rate of spread; 2) a difference in the pattern of patients seeking medical care; 3) differences in clinical staging; 4) differences in ancillary diagnostic aids;

TABLE 3.—Percent of cases under age 65

Country	Male	Female
England	32	34
Finland	63	60
France	70	57
Norway	53	42
United States (Calif., Conn., Mass.)	48	46
United States (Conn.)	51	51
United States (Hospitals)	53	51

TABLE 4.—Percent of cases still localized when first diagnosed

Register	Male	Female
England	36	52
Finland	67	73
France	34	49
Norway	53	84
United States (Calif., Conn., Mass.)	41	53
United States (Conn.)	51	56
United States (Hospitals)	39	56

or 5) various combinations of these factors. Unfortunately, in a study of this scale and type we are not able to distinguish between these hypotheses.

### HISTOLOGICAL CONFIRMATION

The confirmation of a neoplastic change does not necessarily have to be confirmed by a histological section, and this may well be nugatory when the clinical diagnosis is obvious and when there is no intention of treating a patient with advanced disease.

In the United States and Finland and Norway, the advice of a pathologist was usually sought before a patient was further treated. In England, however, only two thirds of the cases were referred for histology, although when the disease was localized and the patient under 65 over 80 percent was referred for histological diagnosis. In France, no distinction was made between cases confirmed by histology and those not confirmed, but since the French register was hospital-based it may be assumed that a large percentage of cases were confirmed.

The treatment of choice for cancer of the tongue in all countries included in this study was radiation. In England 85 percent of male patients had some form of radiation treatment and in Norway 96 percent. Even in Connecticut, where there was a marked preference for surgery, 60 percent of the patients received radiation. Approximately 10 percent of those with the disease were not treated, and almost all of these were patients with advanced disease when diagnosed. There was, however, a considerable difference among the various registers in the use of surgery

TABLE 5.—Percent of cases confirmed by histology when first diagnosed

Register	Male	Female
England	62	69
Finland	90	94
Norway	93	89
United States (Calif., Conn., Mass.)	95	98
United States (Conn.)	93	98
United States (Hospitals)	98	100

TABLE 6.—First course of treatment

Register	Percent of male cases			
	Surgery only	Radiation only	Surgery and radiation	No treatment
England	6	72	13	9
Finland	8	44	35	13
France	4	60	21	16
Norway	2	74	22	2
United States (Calif., Conn., Mass.)	25	56	8	11
United States (Conn.)	33	50	10	7
United States (Hospitals)	17	65	6	12

and radiation. In the European countries surgery was usually followed by a course of radiation, whereas in the United States this was unusual.

In the United States more surgery was performed, and most of it was not supplemented by radiation. It is interesting that in the U.S. Hospital series the types of treatment used were closer to those used in Europe. In England and Wales the English register at this time was biased in favor of radiation, as almost all radiotherapy centers were registering their cases but not all of the main surgical centers were doing so (table 6).

## CHARACTERISTICS OF PATIENTS INCLUDED IN THE STUDY

There were considerable differences in the various registers between the types of patients and the methods of treatment. In England the patients were older, there were more males, their disease was diagnosed at an advanced stage, histological confirmation was often omitted, and almost all had received radiation.

In Finland and Norway the patients were a little younger, the sex ratio was equal, most of the people were seen at an early stage of the disease, and histological confirmation was over 90 percent.

There was some difference in the United States between the population registers and the hospital registers but, in general, the patients were predominantly male, intermediate in age between those in England and Finland and Norway, almost all cases were confirmed by histology, and about one third had had surgery. In France, the patients were younger and their disease was diagnosed at an advanced stage.

## END RESULTS OF TREATMENT

In the protocols used in this work every effort was made to standardize the cases to be included and to ensure uniformity of classification, but nevertheless, certain problems are inherent in a cooperative study of this

type. When we wish to assess the effect of treatment, the main difficulties are: 1) the nonrandom selection of patients for a given type of treatment; 2) the lack of observer error studies in classifying stage of disease; and 3) the lack of knowledge concerning the type of histology in different countries.

The following comments are made, therefore, subject to these reservations concerning the basic data.

Cancer of the tongue, although a disease of advanced age, has a prognosis of about 65 percent survival at 2 years, 50 percent at 5 years, and 45 percent at 10 years if detected while still localized.

The experience reflected in all registers except Finland was that women did better than men. Whether age at first diagnosis has an effect on the relative survival rate is doubtful. Some registers showed an advantage for those under 65, but for Connecticut, Norwegian males, and English females the converse was true. It would seem that age itself is not an important factor to be considered when the differences in relative survival rates are calculated.

## SURGERY

The survival rates of all patients treated by surgery would not be a fair basis for comparison between different countries, as the proportion of patients with advanced disease varies. Consequently, in tables IV a and b (after Conclusions) the calculations were made to show the survival rates for each stage of the disease and for each type of treatment.

It is justifiable to compare the register of England and Wales with the U.S. Central register, as they are incomplete registers, and the Finland and Norway registers with the Connecticut register, as they are complete population registers. But unfortunately, the numbers now become very small; in Norway there were 2 localized cases treated by surgery alone and in Finland 8. Hence, the only possible comparison that remains is that between England and the U.S. Central registers. If this contrast is studied (table 7), then there is no consistent or important difference be-

TABLE 7.—Localized cases only

Register	5-year corrected survival rate (%)	
	Males	Females
England	54	57
Finland	57	52
France	40	52
Norway	41	51
United States (Calif., Conn., Mass.)	52	60
United States (Conn.)	49	61
United States (Hospitals)	47	64



TABLE 8.—5-Year survival rates—cases treated by surgery only

Register	Localized cases		Nonlocalized	
	Male	Female	Male	Female*
England	61	75	26	(—)
U.S. (Central)	69	68	23	22
France	51	63	08	(—)

\* (—) = Too few cases to yield a reliable rate.

tween these two countries, despite the marked difference in the policy of selecting cases for treatment.

Survival rates for cases treated by surgery are significantly better than the survival of all cases, but there is no significant improvement in the United States total survival rate although in this country there was a higher proportion of cases treated surgically. As the cases on the English register were older and less localized, the only conclusion it is permissible to draw from these results is that surgeons can select patients who will have a good prognosis (table 8).

## SURGERY COMBINED WITH RADIATION

Localized cases treated by surgery plus radiation had a poor prognosis compared with surgery alone, which would suggest that surgeons tend to refer their more difficult cases for radiation treatment, but in cases with nonlocalized disease there seemed to be a definite benefit in all cases (table 9).

In England the treatment of preference was radiation and for localized cases English radiotherapists did better than their colleagues in the other countries, but as in the case of the American surgeons it is not permissible to conclude that these successes are the result of treatment rather than the selection of cases for treatment.

In advanced disease, however, there is very little difference between England and the U.S. Central registers, and there are too few cases in the other registers to allow for any comparisons (table 10).

TABLE 9.—5-year survival rates—cases treated by surgery plus radiation

Register	Localized cases		Nonlocalized cases	
	Male	Female	Male*	Female*
England	58	38	31	38
France	57	50	20	32
U.S. (Central)	52	60	30	35
Finland	64	63	(—)	(—)
Norway	67	78	(—)	(—)
Connecticut	78	44	(—)	(—)

\* (—) = Too few cases to yield a reliable rate.

TABLE 10.—5-Year survival rates—cases treated by radiation alone

Register	Localized cases		Nonlocalized cases	
	Male	Female*	Male*	Female*
England	51	61	16	26
France	30	48	07	14
U.S. (Central)	46	50	15	29
Finland	39	32	(—)	(—)
Norway	32	18	11	(—)
Connecticut	28	(—)	4	(—)

\* (—) = Too few cases to yield a reliable rate.

## ANNUAL SURVIVAL RATE

The basic calculation made by the computer was the annual survival rate (Relative R) which gives the survival rate of patients corrected for life-table mortality from one year to the next; from this rate all other rates derive.

As patients live a period of time after the diagnosis of a malignant disease, there is a process of selection, resulting from the early death of those with more malignant disease, so that the less severe cases and those who have been successfully treated remain, and the annual survival rate returns almost to normal. If the survival rates return to normal and no additional patients die of the malignant disease for which they were treated, then it is possible to use the term "cured" for those surviving.

The end results study does not tabulate the causes of death for patients who do die. Consequently, it is not possible to say whether at any time the disease has been eliminated. When, however, the annual survival rate returns to 95 percent of the expected rate and remains there, then the surviving group of patients is relatively free of the disease.

Table VI (after Conclusions) shows the annual survival rates in England and the United States; in Norway and Finland there were not enough cases for this detailed treatment.

In England and the United States the localized cases had a mortality of about 20 percent in the first year and 25 percent in the second year. But in the third year mortality improves, and by the end of the fourth year the male survival rate is above 95 percent.

In the female rate there is a lower mortality rate in the earlier years, and in consequence the survival rate for women is not restored to the above 95 percent level until the fifth year. In advanced disease, the mortality in the first year is nearly 60 percent and in the second year 40 to 50 percent, but if a patient survives the ravages of these 2 drastic years, his chances of survival are greatly improved, and even these advanced cases return to a 95 percent annual survival rate after 4 or 5 years.

Table VII (after Conclusions) demonstrates the annual survival rate in localized diseases treated by surgery or radiation. There is very little difference between surgical patients in England and the United States; the rate for male surgical patients in the United States returns to the 95 percent level more quickly, whereas in England it is the females who do better.

The contrast between surgery and radiation emphasizes that radiation patients do less well in the early years of treatment, but if they do survive the annual rate returns to 95 percent by the end of the fourth year of follow-up.

### SECULAR CHANGES

In England and the United States, statistics were collected for two separate periods to determine whether there had been any secular change in survival rates. Table VIII (after Conclusions) shows that as far as England was concerned there was no difference in the survival rates in the period 1947-48 compared with 1952-53.

The U.S. Central register, however, shows an improvement in the male survival rates, and the Connecticut rate has improved considerably. But the female rates show no real change.

### CONCLUSIONS

Despite large and important differences in the demographic characteristics of patients with cancer of the tongue, there are remarkably few differences in survival rates in countries and in methods of treatment when allowance is made for sex and for stage of the disease when first seen. The one crucial point is to enable the physician or surgeon to start treatment while the disease is still localized.

TABLE I.—Cancer of the tongue, around 1950-1954—5-year corrected survival rates  
(All stages, all ages, all treatments, by histological confirmation)

Sex and country	Number of patients	Confirmed microscopically (%)	5-year corrected survival rates (%)		
			All cases	Confirmed cases only	Not confirmed
<i>Males</i>					
England*	901	62	31	39	16
Finland†	52	90	39	39	30
France‡	4155	N.A.	21	N.A.	N.A.
Norway§	59	93	30	31	—
U.S. (Calif., Conn., Mass.)	534	95	31	31	30
U.S. (Conn.)	165	93	30	29	46
U.S. (Hospitals)	265	98	25	25	22
<i>Females</i>					
England*	346	69	42	46	30
Finland†	48	94	42	45	—
France‡	580	N.A.	38	N.A.	N.A.
Norway§	55	89	45	49	—
U.S. (Calif., Conn., Mass.)	133	98	45	46	—
U.S. (Conn.)	45	98	46	47	—
U.S. (Hospitals)	57	100	44	44	—

\*Data for England covers the period 1952-53.

†Data for Finland covers the period 1953-56.

‡Data for France covers the period 1945-57.

§Data for Norway covers the period 1953-56.

||N.A.=Not available.



TABLE II.—Cancer of the tongue, around 1950–1954—5-year corrected survival rates—confirmed cases only (All stages, all ages, by treatment)

Register and sex	Number of patients	Percent treated by:			5-year corrected survival rates (%)				
		Surgery only	Radiation only	Surgery and radiation	All cases	Surgery only	Radiation only	Surgery and radiation	
<i>Males</i>									
England	525	8	68	20	39	52	38	43	
Finland	47	9	47	38	39	—	28	41	
Norway	55	2	75	24	31	—	23	66	
U.S. (Calif., Conn., Mass.)	507	26	57	8	31	50	26	33	
U.S. (Conn.)	154	34	49	10	29	51	14	30	
U.S. (Hospitals)	259	17	66	7	25	44	24	13	
<i>Females</i>									
England	239	10	64	24	46	69	49	35	
Finland	45	11	40	47	45	—	33	49	
Norway	50	2	50	48	49	—	20	76	
U.S. (Calif., Conn., Mass.)	130	43	37	11	46	57	40	47	
U.S. (Conn.)	44	21	14	6	47	50	59	—	
U.S. (Hospitals)	57	28	58	9	44	69	43	—	

TABLE III.—Cancer of the tongue, around 1950-1954—5-year corrected survival rates (Confirmed and not confirmed, all ages, all treatments, by stage of disease)

Register and sex	Number of patients	Percent localized	5-year corrected survival rates (%)		
			All cases	Local- ized	Not localized
<i>Male</i>					
England	901	36	31	54	17
Finland	52	67	39	57	—
France	4155	34	21	40	10
Norway	59	53	30	41	17
U.S. (Calif., Conn., Mass.)	534	41	31	52	16
U.S. (Conn.)	165	51	30	49	08
U.S. (Hospitals)	265	39	25	47	12
<i>Female</i>					
England	346	52	42	57	24
Finland	48	73	42	52	15
France	580	49	38	52	22
Norway	55	84	45	51	14
U.S. (Calif., Conn., Mass.)	133	53	45	60	25
U.S. (Conn.)	45	56	46	61	16
U.S. (Hospitals)	57	56	44	64	18

TABLE IV (a).—Cancer of the tongue, around 1950–1954—5-year corrected survival rates—Localized Cases Only (Confirmed and not confirmed all ages, by treatment)

Register and sex	Number of patients	Percent treatment			5-year corrected survival rates (%)				
		Surgery only	Radiation only	Surgery and radiation	All cases	Surgery only	Radiation only	Surgery and radiation	
<i>Males</i>									
England	327	9	73	15	54	61	51	58	
Finland	35	11	46	34	57	100	39	64	
France	1425	6	59	28	40	51	30	57	
Norway	31	3	68	29	41	—	32	67	
U.S. (Calif., Conn., Mass.)	220	36	52	5	52	69	46	52	
U.S. (Conn.)	84	44	46	8	49	64	28	78	
U.S. (Hospitals)	103	19	62	6	47	78	43	39	
<i>Females</i>									
England	179	13	66	19	57	75	61	38	
Finland	35	14	43	43	52	76	32	63	
France	285	14	53	24	52	63	48	50	
Norway	46	2	46	50	51	—	18	78	
U.S. (Calif., Conn., Mass.)	71	52	34	10	60	68	50	60	
U.S. (Conn.)	25	56	24	16	61	52	100	44	
U.S. (Hospitals)	32	44	53	3	64	79	55	—	

TABLE IV(b).—Cancer of the tongue, around 1950-1954—5-year corrected survival rates—Not localized cases only (Confirmed and not confirmed, all ages, by treatment)

Register and sex	Percent treatment			5-year survival rates (%)				
	Number of patients	Surgery only	Radiation only	Surgery and radiation	All cases	Surgery only*	Radiation only*	Surgery and radiation*
<i>Males</i>								
England	574	4	71	12	17	26	16	31
Finland	17	0	41	35	00	(—)	(—)	(—)
France	2625	3	65	9	10	08	07	20
Norway	28	0	82	14	17	(—)	11	(—)
U.S. (Calif., Conn., Mass.)	275	17	59	10	16	23	15	30
U.S. (Conn.)	64	16	55	14	08	23	04	(—)
U.S. (Hospitals)	159	16	67	7	12	19	12	(—)
<i>Females</i>								
England	167	2	69	17	24	(—)	26	38
Finland	12	0	42	50	15	(—)	(—)	(—)
France	281	4	50	22	22	(—)	14	32
Norway	9	0	67	11	(—)	(—)	(—)	(—)
U.S. (Calif., Conn., Mass.)	53	30	40	13	25	22	29	35
U.S. (Conn.)	15	33	47	13	16	(—)	(—)	(—)
U.S. (Hospitals)	25	8	64	16	18	(—)	28	(—)

\* (—) = Less than 10 cases.



TABLE V.—Cancer of the tongue, around 1950–1954—5-year corrected survival rates (Confirmed and not confirmed, all treatments, by stage and age)

Register and sex	Localized			Not localized		
	Under 65	Over 65	All ages	Under 65	Over 65	All ages
<i>Male</i>						
England	60	49	54	24	12	17
Finland	71	26	57	00	00	—
France	40	42	40	10	12	10
Norway	40	43	41	08	31	17
U.S. (Calif., Conn., Mass.)	54	49	52	15	17	16
U.S. (Conn.)	47	52	49	04	16	08
U.S. (Hospitals)	48	44	47	16	06	12
<i>Female</i>						
England	57	59	57	30	21	24
Finland	56	43	52	20	—	15
France	55	49	52	23	19	22
Norway	68	31	51	34	—	14
U.S. (Calif., Conn., Mass.)	63	58	60	34	11	25
U.S. (Conn.)	48	74	61	13	20	16
U.S. (Hospitals)	76	46	64	19	20	18

TABLE VI.—Cancer of the tongue, around 1950–1954—annual corrected survival rates (Confirmed and not confirmed, all ages, all treatments, by stage)

Register, sex, stage	Year of follow-up:					
	1st	2d*	3d*	4th*	5th*	6th*
<i>Male localized</i>						
England	81	77	88	96	98	107
France	70	78	86	92	92	94
U.S. (Calif., Conn., Mass.)	80	76	92	96	96	91
U.S. (Conn.)	82	73	90	88	102	85
U.S. (Hospitals)	79	75	85	95	97	99
<i>Male, not localized</i>						
England	42	59	77	95	93	107
France	40	52	73	80	86	91
U.S. (Calif., Conn., Mass.)	44	50	85	88	93	105
U.S. (Conn.)	37	47	83	(—)	(—)	(—)
U.S. (Hospitals)	49	50	77	68	92	89
<i>Female, localized</i>						
England	88	78	87	99	97	106
France	80	80	89	94	98	97
U.S. (Calif., Conn., Mass.)	86	89	89	89	98	104
U.S. (Conn.)	95	85	87	84	105	60
U.S. (Hospitals)	83	99	99	76	103	103
<i>Female, not localized</i>						
England	42	70	88	88	105	105
France	51	65	73	98	90	100
U.S. (Calif., Conn., Mass.)	45	67	89	95	94	81
U.S. (Conn.)	34	(—)	(—)	(—)	(—)	(—)
U.S. (Hospitals)	37	70	(—)	(—)	(—)	(—)

\* (—) = Less than 10 survivors.

TABLE VII.—Cancer of the tongue, around 1950–1954—annual corrected survival rates (Confirmed and not confirmed, all ages, localized cases only, by treatment)

Register, sex, stage	Years of follow-up:					
	1st*	2d*	3d*	4th*	5th*	6th*
<i>Male, surgery</i>						
England	93	86	87	87	100	108
France	68	89	91	95	94	96
U.S. (Calif., Conn., Mass.)	91	86	93	96	97	92
U.S. (Conn.)	84	83	95	95	99	84
U.S. (Hospitals)	93	86	90	103	103	103
<i>Male, radiation</i>						
England	80	76	86	98	97	108
France	66	70	82	89	91	94
U.S. (Calif., Conn., Mass.)	76	75	91	95	94	89
U.S. (Conn.)	84	60	79	(—)	(—)	(—)
U.S. (Hospitals)	77	73	86	98	93	101
<i>Female, surgery</i>						
England	88	84	105	100	93	100
France	86	95	96	96	96	96
U.S. (Calif., Conn., Mass.)	90	94	93	83	105	78
U.S. (Conn.)	96	88	85	(—)	(—)	(—)
U.S. (Hospitals)	95	102	94	84	103	(—)
<i>Female, radiation</i>						
England	89	81	89	99	97	106
France	76	79	91	89	98	95
U.S. (Calif., Conn., Mass.)	78	86	90	96	86	(—)
U.S. (Conn.)	(—)	(—)	(—)	(—)	(—)	(—)
U.S. (Hospitals)	78	95	103	69	(—)	(—)

\* (—) = Less than 10 survivors.

TABLE VIII.—Cancer of the tongue—5-year survival rates (all histology, all ages, all treatments, localized cases only, by time period)

Register and sex	1945–49	1950–54
<i>Male</i>		
England	54	54
U.S. (Calif., Conn., Mass.)	49	52
U.S. (Conn.)	39	49
U.S. (Hospitals)	57	47
<i>Female</i>		
England	58	57
U.S. (Calif., Conn., Mass.)	62	60
U.S. (Conn.)	62	61
U.S. (Hospitals)	71	64

## SUMMARY

An international comparison was made of patients with cancer of the tongue who were registered in England, Finland, Norway, and the United States. Differences were found in the characteristics of the patients and in the type of treatment used.

1) Patients with localized disease have better survival rates than those with advanced disease.

2) Female survival rates are better than males.

3) Age is not an important factor in prognosis.

4) Patients treated by surgery have better survival rates than others, but it has not been possible to eliminate the effect of bias in the selection of patients for surgery.

5) Countries in which surgery for cancer of the tongue is most widely practiced do not necessarily show better over-all survival rates.

6) Differences between countries are due more to differences in the stage of the disease when first seen, rather than to differences in type of treatment.

7) If a patient survives 4 years after initial diagnosis, further prognosis is good.

8) There is no evidence of a secular improvement in survival rates between the late 1940's and the early 1950's.





## Malignant Tumors of the Tongue Treated at the Norwegian Radium Hospital, 1932-1958

ERIK POPPE, *Norwegian Radium Hospital, Oslo, Norway*

SINCE the opening of the Norwegian Radium Hospital in 1932, the number of patients with cancer of the tongue has been about 25 per year. During the 27-year period from 1932-58, 599 patients were admitted. In 549 cases the clinical diagnosis was verified by histological examination. Almost all the tumors histologically examined were squamous cell carcinomas. Only 7 represented other forms of malignant tumors. Most of the patients were men: 364 (60.8%). There were 235 women patients (39.2%). The average age of the patients was about the same in both sexes, 63 years.

The frequency of clinically demonstrable metastases on first admission to the Norwegian Radium Hospital was 31 percent in the total material, 37 percent in men and 20 percent in women. Distribution according to tumor size on admission has been practically the same for the years 1932-58. Large tumors are more frequent in men.

The follow-up has been 100 percent. All the admitted patients are included:

Males:	Five-year crude survival (%)
Without metastases	37
With metastases	8
Females:	
Without metastases	48
With metastases	14
Total material:	22

Five-year survival rates in relation to location of the primary tumor were: free part of the tongue, 25 percent; base part of the tongue, 13 percent. There is no statistically significant difference in the therapeutic results from 1932-58.

## Summary of General Discussion

Based on material collected by the Ad Hoc Group and data presented by the named discussants, the discussion covered the following main points:

1. (a) The possible importance of variations in the proportion of cases localized to the anterior two thirds and posterior one third of the tongue between the two sexes and between countries was emphasized by a number of discussants. That such differences in localization within the tongue exist between various geographical regions in some countries has already been demonstrated in epidemiological studies. The question was raised whether such differences could serve to explain some of the disparities observed in corrected survival rates within the same treatment categories.  
(b) It was pointed out that tumors originating in the posterior one third differed from tumors originating in the anterior two thirds of the tongue, both in regard to pathologic characteristics and mode of spread. Also, that tumors in the posterior part of the tongue were treated by other techniques than were tumors in the anterior part of the organ.  
(c) Reference was made to the possible influence, on the comparability of survival rates between countries (and/or between clinics), of differences in the accuracy with which tumors originating in the posterior part of the tongue are separated from tumors in adjacent parts of the mesopharynx.
2. The possibility of differences in prognosis for tumors associated with different carcinogenic factors was mentioned.
3. The evaluation of the results of various treatment techniques through clinical trials was discussed. Opinion differed as to whether such a trial could be defended on ethical grounds. It was pointed out that because of the relative low incidence of cancer of the tongue, it would be difficult to get a sufficient number of cases to carry out a clinical trial.
4. It was emphasized that in the choice of treatment techniques the quality of survival as well as survival rates should be considered.

## **Cancer of the Esophagus**

End Results in Cancer of the Esophagus. G. J. A. JOHNSON and L. LIPWORTH, England

Malignant Tumors of the Esophagus Treated at the Norwegian Radium Hospital, 1932-1961. ERIK POPPE, Norway

### **GENERAL DISCUSSION**

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Presented at the International Symposium on End Results of Cancer Therapy, Sandefjord, Norway, September 16-20, 1963.





## End Results in Cancer of the Esophagus

G. J. A. JOHNSON and L. LIPWORTH, *Medical Statistician, General Register Office, London, England*

IN this study a total of 12,046 patients diagnosed as having cancer of the esophagus at various periods between 1945 and 1957 have been included in series provided by cancer registries in France, Finland, Norway, the United States, and England and Wales. The returns of the Connecticut registry are included in those of the U.S. Central figures but analyzed separately because of completeness of coverage in Connecticut.

The incompleteness of registration in England, the United States, and France made it impossible to assess from these morbidity data the incidence of cancer of the esophagus in all the five contributing countries but, owing to the very poor prognosis of the disease, an estimate could be obtained from mortality statistics (table 1).

Table 1 shows considerable variations in mortality rates between the five countries and also between the sexes in each country.

### SEX

The sex ratios in the various registers followed much the same pattern as in the crude mortality rates of the countries involved. They increased from 50 percent males in the Finnish register to some 80 percent in the

TABLE 1.—Death rates, all ages, 1952–56 (WHO Epidemiology and Vital Statistics Report, vol. 12, 1959)

Country	Males		Females	
	Crude	Standardized	Crude	Standardized
United States (white)	39.8	41.8	10.7	10.4
Norway	42.1	40.8	15.1	12.3
England and Wales	64.4	60.5	39.7	28.6
Finland	71.4	108.8	68.4	63.3
France	136.9	126.8	20.8	13.7

TABLE 2.—Proportion of male cases in each register

Register	Period	Percent males	2 × SE
Finland	1953-56	50	3.1
England and Wales	1948-49,	65	1.8
	1952-53		
Norway	1953-56	74	4.5
U.S. Hospitals	1945-54	82	3.1
U.S. Central	1945-54	83	1.8
Connecticut	1945-54	85	2.6
France	(1945-57)	93	0.7

American and 93 percent in the French registers. Without further breakdown into incidence at various levels of the esophagus, it is difficult to draw any conclusions from these figures (table 2).

### HISTOLOGICAL CONFIRMATION

The proportion of cases confirmed by histology varied from 39 percent in the Finnish series to 86 percent in the U.S. Hospital cases. If patients not subjected to surgery were considered, the proportion, so confirmed, was still nearly 80 percent in the U.S. registries and 40 to 60 percent in the four European registries. However, the U.S., Finland, and Norway registries gave histological analyses for over 90 percent of surgically treated patients, so that, to avoid a bias toward surgically treated patients, the following analysis will relate to both confirmed and not confirmed cases, with reference to not confirmed cases where appropriate (table 3).

### AGE

In the Norwegian series the percentages of males and females aged 70 and over (55 and 59%, respectively) were significantly higher than in the other registers, where the corresponding proportions ranged from 43 per-

TABLE 3.—Proportion of (a) all cases and (b) surgically treated cases confirmed by histology

Register	Period	Percentage confirmed histologically	
		All cases	Surgical cases
Finland	1953-56	39	100
England and Wales	1948-49	62	76
	1952-53		
Norway	1953-56	69	97
Connecticut	1945-54	77	94
U.S. Central	1945-54	81	97
U.S. Hospital	1945-54	86	98
France	1945-57	49	50

TABLE 4.—Percentage of cases in each register aged 70 and over

Register	Period	Males	Females
Norway	1953-56	55	59
England and Wales	1948-49,	43	33
	1952-53		
Connecticut	1945-54	34	39
U.S. Central	1945-54	34	37
Finland	1953-56	33	45
U.S. Hospital	1945-54	24	30
France	1945-57	13	24

cent for England and Wales to 13 percent for the French register in males and from 45 percent for Finland to 24 percent for the French register in females (table 4).

The small proportion of older males with carcinoma of the esophagus in the French registry figures is interesting. Comparison with other registries is obviously highly significant, and examination of World Health Organization (WHO) age-specific death rates in 1952-56 confirms that the higher mortality from this condition among French males is largely due to greater incidence in younger age groups.

## STAGE

The proportion of localized cases in males at all ages did not differ much from that in females in any of the registers, although in all registers except Connecticut (1950-54), it was slightly higher in the females.

In both sexes the percentage of localized cases varied from 4 percent in the French and 18 percent in the England and Wales registers to about 60 to 70 percent in the Finland and Norway registers, the U.S. Central register showing 29 percent (table 5). These differences are not reflected in the Finland and Norway survival figures and may be due to different methods of staging.

TABLE 5.—Percentage of localized cases in each period by register and sex (all ages—confirmed and not confirmed)

Register	Period	Males	Females
England and Wales	1948-49	14	19
	1952-53	19	22
Finland	1953-56	57	59
Norway	1953-56	60	69
U.S. Central	1945-49	31	31
	1950-54	27	30
U.S. Hospital	1945-49	11	17
	1950-54	22	27
Connecticut	1945-49	43	54
	1950-54	33	29
France	1945-57	4	5

The small proportion of early cases in the French figures is partly due to selection, as registration in France is largely confined to specialized "anti-cancer" centers, to which the more advanced cases are likely to be referred.

## CHOICE OF TREATMENT 1950-1956 (FRANCE 1945-1957)

### Localized Cases

Sixty-five and 70 percent of the younger male and female patients, respectively, registered in England and Wales in 1952-53 as having localized cancer of the esophagus were treated by surgery. Perhaps these figures, which are much higher than in any of the other registers, were due to the more exclusive definitions of staging used in England and Wales. Certainly table 6 shows that only one fifth of their cases was classified as localized. Of the older patients registered in England and Wales, 31 percent of males and 44 percent of females received surgery.

Among the localized cases registered in the U.S. Central series in 1950-54, surgery was used in 30 percent of the younger males and in 25 percent of those 70 or more years of age. In the corresponding groups of females the percentages were 48 and 18, respectively, but the numbers involved were very small.

Only a negligible proportion of the Finland and Norway patients received surgery, and apparently the number in this treatment category in the French figures was too small to be analyzed.

Of those patients receiving treatment, radiotherapy was used in the vast majority of localized cases on the French, Finnish, and Norwegian registers. Equally, in the England and Wales and U.S. Central registries where, as has been shown, fair proportions were treated by sur-

TABLE 6.—Percentage of localized cases in each period, register, sex, and age group (confirmed and not confirmed)

Register	Period	Males		Females	
		Under 70	70 and over	Under 70	70 and over
England and Wales	1948-49	16	10	19	19
	1952-53	19	18	20	26
Finland	1953-56	57	56	62	55
Norway	1953-56	46	72	68	71
U.S. Central	1945-49	29	34	26	41
	1950-54	26	31	28	33
U.S. Hospital	1945-49	11	13	12	29
	1950-54	20	26	22	39
Connecticut	1945-49	41	48	53	56
	1950-54	33	32	31	26
France	1945-57	4	4	6	4



gery alone, the only remaining tumor-directed treatment used in reasonable proportions was radiotherapy. While the number of men in which surgery plus radiotherapy, hormone treatment, or chemotherapy was given was negligible in all registers, the proportion of cases in which no known treatment at all was undertaken was depressingly high, particularly in Finland where half the younger patients and over 80 percent of the older patients in the localized group were in this category (table 7).

#### Not Localized Cases

In the more advanced cases only about 60 percent of the patients of both sexes in the England and Wales and U.S. Central registers were shown as having some form of tumor-directed treatment. In England and Wales this was divided almost equally between surgery and radiotherapy, while in the U.S. Central register rather more were treated with surgery than with radiotherapy.

Fifty-nine percent of the patients on the French register with advanced growths of the esophagus were given radiation therapy and a further 26 percent surgery, with or without radiotherapy.

The figures for Finland show that only about one fifth of the more advanced cases received tumor-directed treatment and this almost entirely in the form of radiotherapy.

In Norway 23 percent of all younger males and 36 percent of the younger females with advanced disease were treated by surgery. Comparison with the corresponding sex-age groups in localized cases of this registry where very little surgery was done is significant in each case ( $P < 0.01$  in males,  $P < 0.05$  in females). This is not altogether surprising since the type of treatment is dictated by site in the esophagus as well as by stage (table 8).

### END RESULTS

In the analysis which follows, figures will relate to combined confirmed and not confirmed cases, except where a reference to confirmed cases is specified. Also, the references to the England and Wales and the U.S. registers will relate to the later periods, except where otherwise indicated.

Whenever any large group of figures is provided, the survival is poor irrespective of stage and treatment. Examination of the survival curve for all cases, not broken down into stage or age group, shows that 80 to 90 percent of the patients died in the first year and that more than half of the remainder were dead by the end of the second year. For the few patients still alive after this period there was a better outlook, about one third to one half of the patients in the larger registries being alive after the next 3 years.

TABLE 7.—Percentage distribution of treatment in localized cases by sex and age in each register (confirmed and not confirmed)

Sex	Register	Period	Age group	Surgery	Radiotherapy	Surgery and radiotherapy	Chemotherapy/hormone	No known treatment
Males	England and Wales	1952-53	0-69	65	20	2	1	12
	Finland	1953-56	70+	31	28	4	7	31
	Norway	1953-56	0-69	3	40	2	—	55
			70+	1	17	—	—	82
			0-69	5	80	2	—	14
			70+	4	67	—	—	29
	U.S. Central	1950-54	0-69	30	30	4	—	36
	U.S. Hospital	1950-54	70+	25	28	4	—	43
	Connecticut	1950-54	0-69	38	20	8	—	35
	France*	1945-57	70+	37	26	5	—	32
Females			0-69	25	29	7	—	40
			70+	26	23	8	—	44
			0-69	—	75	—	—	—
			70+	—	—	—	—	—
	England and Wales	1952-53	0-69	70	15	3	—	12
	Finland	1953-56	70+	44	21	2	4	29
	Norway	1953-56	0-69	2	44	2	—	53
			70+	—	11	1	—	88
			0-69	7	70	—	—	22
			70+	—	44	2	—	54
	U.S. Central	1950-54	0-69	48	11	4	—	37
	U.S. Hospital	1950-54	70+	18	27	5	—	50
	Connecticut	1950-54	0-69	56	22	—	—	22
			70+	14	29	14	—	43
			0-69	50	—	10	—	40
			70+	29	—	14	—	57
	France*	1945-57	0-69	—	—	—	—	—
			70+	—	—	—	—	—

\*The methods of treatment analyzed in the French returns are confined to those where numbers are sufficient to be of statistical value. There were only 17 females with localized tumor.

TABLE 8.—Percentage distribution of treatment in not localized cases by sex and age in each register (confirmed and not confirmed)

Sex	Register	Period	Age group	Surgery	Radio-therapy	Surgery and radiotherapy	Chemotherapy/hormone	No known treatment
Males	England and Wales	1952-53	0-69	30	29	4	4	34
	Finland	1953-56	70+	19	21	3	10	48
	Norway	1953-56	70+	2	19	2	—	77
	U.S. Central	1950-54	70+	—	15	—	—	85
	U.S. Hospital	1950-54	70+	23	46	5	—	26
	Connecticut	1950-54	70+	6	44	3	—	47
	France	1945-57	70+	31	22	6	—	41
				27	22	1	—	50
				40	21	6	1	32
				40	10	3	—	48
Females	England and Wales	1952-53	0-69	34	28	5	2	31
	Finland	1953-56	70+	28	19	4	14	36
	Norway	1953-56	70+	1	29	—	—	69
	U.S. Central	1950-54	70+	—	15	—	—	85
	U.S. Hospital	1950-54	70+	36	18	27	—	18
	Connecticut	1950-54	70+	39	14	14	—	71
	France	1945-57	70+	35	23	6	—	37
				33	19	—	—	39
				43	20	—	—	47
				21	14	—	—	43

All registers, except Finland, showed better results for females than for males. The large group of Finnish women had the same poor prognosis as did the males; in fact the year-by-year corrected survival was practically identical. If the two stages are combined, a comparison with figures from the England and Wales register shows that the 1-year survival of both sexes in Finland was better than that of males and similar to that of females in the England and Wales register. In subsequent years, however, the corrected survival ratios of both males and females in the Finnish registry fell below those for England and Wales to a marked extent, and at the end of 5 years there was a statistically significant difference in the experience of females for the whole period in the two registers ( $P < 0.01$ ). Since the 1-year survival of both sexes in Finland and the 5-year survival of males compared reasonably well with that of other registers, the poor 5-year adjusted survival of Finnish females was probably due not to quality of treatment but to some epidemiological factor, possibly related to the high incidence of esophageal cancer in females in Finland. A study of incidence at different levels of the esophagus may be revealing.

The stage of the disease also affected the results—the outlook being particularly poor for the more advanced cases. For localized cases, the 5-year corrected survival rates in males, confirmed and not confirmed by histology, ranged from 10 percent in England and Wales and 5 percent in the U.S. Central register to 2 percent and 1 percent in the French and Norwegian registers, respectively.

Because of the poor prognosis in this neoplasm, it is perhaps worth while to examine the corrected 1-year survival for this stage. For males the figures for the French and England and Wales registries are 29 percent and 28 percent, respectively, and less in the other registries, dropping to 18 percent in Norway. In the French register the comparatively good survival of the early cases in the first 12 months is significantly different from that of the advanced cases ( $P < 0.01$ ). The survival of these localized cases continued to be better in the second and third years, but in the subsequent 2 years the situation was reversed so that the total 5-year corrected survival for both stages in the French males was almost identical. This could be explained by the reduction of the 182 localized cases to only 9 by the commencement of the fourth year, with a corresponding increase in the variance of the annual survival, and reveals how misleading a 5-year survival rate can be in malignant disease with heavy mortality (table 9).

In females the 5-year corrected survival in patients with early disease varied from 3 percent in Finland to 14 percent in the U.S. Central register—that is, if small groups of less than 20 patients are ignored. Survival in females was better than in males, except in Finland where no difference was observed.



TABLE 9.—Cancer of the esophagus (males)—confirmed and not confirmed: corrected 1-year and 5-year survival rates

	France 1945-57		Connecticut 1950-54		England and Wales 1952-53		Finland 1953-56		Norway 1953-56		U.S. Central 1950-54		U.S. Hospital 1950-54	
	Local- ized	Not local- ized	Local- ized	Not local- ized	Local- ized	Not local- ized	Local- ized	Not local- ized	Local- ized	Not local- ized	Local- ized	Not local- ized	Local- ized	Not local- ized
1-year corrected survival	28.8 ± 7.0	17.7 ± 1.2	15.0 ± 6.9	14.4 ± 5.4	28.0 ± 7.0	9.1 ± 2.1	21.1 ± 4.9	13.5 ± 5.5	18.1 ± 6.1	14.4 ± 7.4	21.1 ± 5.8	15.2 ± 3.4	25.9 ± 11.8	21.7 ± 6.2
5-year corrected survival	2.4 ± 4.2	2.1 ± 0.6	3.2 ± 3.9	2.2 ± 2.5	9.7 ± 5.4	2.0 ± 1.2	2.5 ± 2.2	0.8 ± 1.6	1.2 ± 2.2	1.2 ± 2.5	4.7 ± 3.5	2.3 ± 1.6	4.6 ± 6.3	0.6 ± 1.3
Number of cases	182	3,823	112	178	176	765	295	162	169	93	209	458	59	181

In the advanced cases, on the other hand, the 5-year corrected survival rate in males was 2 percent in the England and Wales, U.S. Central, and French registers and less elsewhere. The relative survival over the first year was 14 to 15 percent in the French, Finland and Norway, and U.S. Central registries and 9 percent in that of England and Wales. In this stage the experience of female patients is not noticeably better.

The effect of age on the results within the various sex-stage groups of the different registers was not consistent enough to justify any firm conclusions, though the 1-year corrected survival was consistently better in younger males in both stages.

### Results of Different Forms of Treatment

Examination of results obtained by different types of treatment revealed that surgery was followed by the most favorable survival, but this may have been due to selection. In the England and Wales and U.S. Central registers, where the number of cases treated by surgery were large enough to analyze, the 5-year corrected survival was 13 to 14 percent for males with localized disease and roughly half this for the more advanced cases. So few cases were treated by surgery in Finland and Norway—32 males in all—that an analysis was impracticable. Five-hundred fifty-four male patients with advanced growths were treated by surgery in France, with a 5-year corrected survival of 3.3 percent. This was slightly better than their results for all forms of treatment of esophageal malignancy whether localized or advanced (2.4 and 2.1, respectively), but the differences are not significant.

Surgery also produced the best results in females for whom the large numbers in the England and Wales register showed corrected 5-year survival rates about 4 percent higher in each stage than those for males. The numbers elsewhere were too small to warrant reasonable analysis.

Likewise, the patients receiving radiotherapy had better results than did patients in the same stage and age groups who remained without treatment, particularly in the survival for the first 12 months after treatment, which, for example, in males with localized disease, varied from 30 percent in Finland to 17 percent in the U.S. Central registry after radiotherapy, and never exceeded 15 percent where no known treatment was given. Again, this may have been influenced by selection.

There were only 3 known survivors at 5 years among a total of 639 patients treated by surgery plus radiotherapy in all the participant countries. Most of these patients were beyond the localized stage at diagnosis, although their survival in the first 12 months varied between 15 to 21 percent in the larger registries. This, again, was better than the corresponding figures for those who had no known treatment.

There were also no 5-year survivors in a total of 85 patients who received only chemotherapy or hormones, 6 percent of whom survived 1 year. Only 8 patients in this group had localized disease.

Examination of the experience of those who had survived 1 year after treatment, or after being seen at a hospital, which is an effectively similar period in those who had had no known treatment at all, was not very rewarding due to the small numbers involved following the heavy death rate in the first 12 months. In Finland the 1- to 5-year corrected survival was 4.8 percent (46 patients surviving the first year) for males not given treatment, compared to 10.7 percent (88 cases) for all males. In Finnish females, where the numbers affected were similar, the survival was 11.9 percent in the untreated against 10.1 percent for all females in the 1- to 5-year period. However, these survivals are all small when compared with the larger registries for the corresponding period. In England and Wales, for example, it was 26 to 27 percent in both treated and untreated males, but the latter comprised only 15 cases in all. There was thus no evidence to show whether having had treatment affected the prognosis, once the patient had survived a year.

#### Changes Over Time in the England and Wales and U.S. Registers

In considering any trends in the England and Wales figures, it must be mentioned that a greater proportion of cases were notified by Radiotherapy Centers during 1948-49 than during 1952-53. This would account for a higher percentage of advanced cases in the earlier period (table 10).

In the U.S. Central register, although the percentage of localized cases decreased in their 1950-54 series, compared with 1945-49, the corrected survival at both 1 year and 5 years improved (table 11).

With regard to different types of treatment, improvement in the survival of males after surgery was evident in both stages, in the England and Wales and the U.S. Central registers. The improvement in the relative 5-year survival rate from 1 to 9 percent in the males of the U.S. Central register was statistically significant ( $P=<0.01$ ).

In the large number of females in the England and Wales register treated by surgery the improvement was also apparent. The 5-year

TABLE 10.—Proportion of not localized cases registered in England and Wales in 1948-49 and 1952-53

Period	Proportion of not localized cases		
	Males	Females	Persons
1948-49	86	81	84
1952-53	81	78	80

TABLE 11.—Proportion of localized cases registered by U.S. Central in 1945-49 and 1950-54, and 1- and 5-year corrected survival rates for all cases registered in the two periods

Period	Males			Females		
	Proportion localized	1-Year corrected survival (all cases)	5-Year corrected survival (all cases)	Proportion localized	1-Year corrected survival (all cases)	5-Year corrected survival (all cases)
1945-49	31	0.116	0.010	31	0.156	0.047
1950-54	27	0.169	0.028	30	0.213	0.057

TABLE 12.—Five-year corrected survival rates by sex and stage for cases treated by surgery: England and Wales (1948-49 and 1952-53) and U.S. Central (1945-49 and 1950-54)

England and Wales				U.S. Central			
Period	Localized	Not localized	All stages	Period	Localized	Not localized	All stages
MALES							
1948-49	0.069	0.039	0.045	1945-49	0.000	0.016	0.011
1952-53	0.132	0.048	0.075	1950-54	0.141	0.075	0.092
FEMALES							
1948-49	0.122	0.019	0.055	1945-49	*	*	0.177
1952-53	0.176	0.097	0.124	1950-54	*	0.67	0.157

\*Under 20 cases at risk.

TABLE 13.—Five-year corrected survival rates by sex and stage for cases treated by radiotherapy: England and Wales (1948-49 and 1952-53) and U.S. Central (1945-49 and 1950-54)

England and Wales				U.S. Central			
Period	Localized	Not localized	All stages	Period	Localized	Not localized	All stages
MALES							
1948-49	0.057	0.015	0.024	1945-49	0.000	0.000	0.000
1952-53	0.071	0.013	0.023	1950-54	0.021	0.000	0.013
FEMALES							
1948-49	0.091	0.023	0.038	1945-49	*	*	0.000
1952-53	0.058	0.077	0.074	1950-54	*	0.000	0.000

\*Under 20 cases at risk.



TABLE 14.—Percentage of cases by sex and stage receiving no known treatment: England and Wales (1948-49 and 1952-53) and U.S. Central (1945-49 and 1950-54)

England and Wales				U.S. Central			
Period	Localized	Not localized	All stages	Period	Localized	Not localized	All stages
MALES							
1948-49	16	44	40	1945-49	60	67	67
1952-53	20	40	36	1950-54	39	44	46
FEMALES							
1948-49	10	41	35	1945-49	60	49	57
1952-53	19	33	30	1950-54	43	38	45

corrected survival ratio in not localized cases increased from 2 to 10 percent; this was also statistically significant ( $P < 0.05$ ) (table 12).

Radiotherapy was followed by no marked improvement in the England and Wales figures, except in females with advanced disease, where the 5-year corrected survival rate increased from 2 to 8 percent, but this difference was not statistically significant. About 100 patients were at risk in each period.

No trend was obvious in the smaller series of American patients treated with radiotherapy (table 13).

The proportion of cases receiving no known treatment decreased by about 5 percent in the England and Wales register in the two periods, while in the U.S. Central register it fell by as much as 20 percent in males and 12 percent in the small number of females (table 14).

## SUMMARY

The end results in 12,046 cases of cancer of the esophagus registered in France, the United States, Finland, Norway, and England and Wales in 1945-57 are discussed.

Surgery was used extensively in localized cases in England and Wales, to a lesser degree in the United States, and rarely in Finland and Norway or France where radiation was predominant.

A depressingly large proportion of patients were shown to have had "no known treatment"—for example, 40 percent of males with localized disease in the U.S., England and Wales, and Finland and Norway registries.

The results confirmed the poor prognosis usually associated with this condition—80 to 90 percent of patients dying in the first 12 months. Localized cases fared better than the advanced ones and females showed a moderately better survival than males.

A separate examination of end results at different levels of the esophagus might explain some of the features of these results.



## **Malignant Tumors of the Esophagus Treated at the Norwegian Radium Hospital, 1932-1961**

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ACCORDING to the figures from the cancer registry, an average of 96 cases of malignant tumors in the esophagus have been registered yearly in Norway during 1953-59. Among these, an average of 72 were men and 24 were women, which corresponds to 2.1 percent of all malignant tumors in men and 0.7 percent of all malignant tumors in women.

During 1932-61, a total of 833 patients with malignant tumors in the esophagus have been treated at the Norwegian Radium Hospital. In the last 5 years the average number of patients has been 42 or approximately one half of the total number of patients reported to the cancer registry for the entire country. All the patients got their primary treatment at the hospital, and none were treated for recurrences or metastases after primary treatment elsewhere.

About 80 percent of the patients were men and about 20 percent women. Most of the patients were from 50 to 80 years of age and only 3 were younger than 40.

The frequency of metastases on first admission to the Norwegian Radium Hospital has apparently been low. This depends on the difficulty in demonstrating metastases by clinical examination—16.6 percent of the total patients had clinically demonstrable metastases on admission; 17.1 percent of the men; and 14.1 percent of the women.

The diagnosis was verified by histologic examination in 71 percent of the cases. Squamous cell carcinoma was found in 83 percent of the histologically verified cases. The rest were adenocarcinomas, anaplastic carcinomas, and unspecified malignant tumors.

The principal treatment was by external irradiation. Surgical treatment of the primary tumor was performed in a few patients with adenocarcinoma in the lower third of the esophagus. All the patients with squamous cell carcinoma and the rest of the patients with adenocarcinoma

were treated by external irradiation. Gastrostomy was performed only when parenteral feeding and irradiation failed to restore the patient's general condition or to improve the esophageal obstruction.

The palliative results of the treatment have usually been very satisfactory, with relief of the esophageal obstruction and improvement of the general condition. Among the patients without clinically demonstrable metastases 20 percent of the men and 25 percent of the women were alive 12 months after the treatment. Of the patients with clinically demonstrable metastases on admission, 7 percent of the men and 18 percent of the women were alive after 12 months.



## Summary of General Discussion

The discussion of the papers on the survival experience of patients with malignant tumors of the esophagus covered the following main points:

1. Some discussants questioned the comparability of survival data in esophageal cancer when there was no information about the proportion of cases originating in different parts of the esophagus, as major disparities exist in cell types, mode of spread, and treatment possibilities between tumors in the upper, middle, and lower part of the organ. It was said to be desirable to make studies on the distribution of tumors within the esophagus, in various countries and in both sexes, to see if differences in this factor would serve to explain dissimilarities in survival experience. The importance of such studies in identifying etiological factors was also emphasized. It was pointed out that some studies already undertaken had not shown any difference in the sex ratio in tumors localized to different parts of the esophagus.
2. The difficulties involved in obtaining uniformity in the staging of tumors of the esophagus were emphasized by a number of participants. It seemed that the most common practice has been to base the staging on all available information obtained during the first course of treatment in treated cases. It was stressed that particular difficulties arose in differentiating between truly localized cases, and cases with spread to local lymph nodes or direct invasion of adjacent tissue in cases not treated by surgery. Doubt was expressed whether intensive efforts for more differentiated staging would yield very much.
3. The question was raised whether comparability of data could be improved by staging surgical cases without taking into consideration observations made during surgical intervention and/or from pathological reports on surgical specimens. This would improve the comparability with series treated radiologically, in which such information would not be available.
4. Special caution is necessary in comparing treatment results from various clinical materials, because of a number of factors influencing not only the selection of patients to various treatment categories but also the selection of patients entering specific clinics.
5. There was some discussion on the desirability of extensive surgery and particularly of various palliative treatments given to older patients with tumors of the esophagus. There seemed to be no general agreement on this subject.



## **Cancer of the Stomach**

Survival of Patients With Cancer of the Stomach. EINAR PEDERSEN, Norway  
Surgery for Gastric Cancer at the University of Minnesota Medical Center,  
1936 Through June 30, 1958. OWEN H. WANGENSTEEN and VICTOR A.  
GILBERTSEN, USA

The Second-Look Operation for Abdominal Malignancies, 1948-1963. WARD  
O. GRIFFEN, JR., VICTOR A. GILBERTSEN, and OWEN H. WANGENSTEEN, USA

### **GENERAL DISCUSSION**

#### **Moderator**

JOHANNES CLEMMESSEN, Denmark

#### **Rapporteur**

TORBJØRN MØRK, Norway

#### **Discussants**

GEORGE CRILE, JR., USA

SIDNEY J. CUTLER, USA

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VICTOR GILBERTSEN, USA

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Presented at the International Symposium on End Results of Cancer Therapy,  
Sandefjord, Norway, September 16-20, 1963.





## Survival of Patients With Cancer of the Stomach

EINAR PEDERSEN, *Director, The Cancer Registry of Norway, Norwegian Radium Hospital, Oslo, Norway*

THERE are many publications showing the generally grave prognosis in stomach cancer and one may wonder whether there is any justification for adding to the already existing volume of depressing evidence. However, the material on which the present report is based has some unusual features, apart from the large number of cases involved.

### MATERIAL

*Sources of data.*—The material contributed by Denmark, England and Wales, Finland, France, Norway, and the United States comprises more than 40,000 cases of stomach cancer (table 1). There are some important differences in the sources of the data for the various countries.

In Denmark, Finland, and Norway, and in Connecticut, United States, the materials were obtained by means of presumably very efficient, but not identical, cancer registration schemes covering the entire populations and striving to include all diagnosed cases of cancer.

The data from England and Wales combine case reports from hospitals in several hospital regions. The 5,646 cases included in the analysis for the years 1952–53 correspond to approximately 20 percent of the recorded number of deaths from stomach cancer in England and Wales in the same years.

The French data are based on cases seen in the 22 regional cancer treatment centers.

Data from the United States, apart from the Connecticut material mentioned, are presented under two different headings: U.S. Central registries refers to the combined data from centralized registries in California, Connecticut, and Massachusetts, while U.S. Teaching Hospitals designates the pooled material of five teaching hospitals. Neither of these two hospital series can be related to a defined population base.

TABLE 1.—Cancer of the stomach: number of cases, by age, sex, country, and years of diagnosis

Country and years of diagnosis	0-59 years		60 years and over		Total
	Number	Percent	Number	Percent	
MALES					
Denmark, 1950-54	956	27. 2	2561	72. 8	3517
England and Wales, 1948-49	1287	43. 1	1697	56. 9	2984
1952-53	1335	37. 7	2205	62. 3	3540
Finland, 1953-56	1384	38. 5	2210	61. 5	3594
France, 1945-57	395	48. 8	414	51. 2	809
Norway, 1953-56	829	24. 0	2625	76. 0	3454
United States					
Connecticut, 1945-49	309	31. 4	676	68. 6	985
1950-54	300	29. 2	726	70. 8	1026
Central registries, 1945-49	775	30. 9	1736	69. 1	2511
1950-54	672	28. 0	1730	72. 0	2402
Teaching Hospitals, 1945-49	186	39. 5	285	60. 5	471
1950-54	189	34. 2	364	65. 8	553
FEMALES					
Denmark, 1950-54	508	24. 2	1590	75. 8	2098
England and Wales, 1948-49	673	38. 7	1066	61. 3	1739
1952-53	682	32. 4	1424	67. 6	2106
Finland, 1953-56	841	28. 4	2117	71. 6	2958
France, 1945-57	210	45. 4	253	54. 6	463
Norway, 1953-56	493	21. 0	1859	79. 0	2352
United States					
Connecticut, 1945-49	176	30. 7	398	69. 3	574
1950-54	140	24. 4	435	75. 6	575
Central registries, 1945-49	410	31. 3	899	68. 7	1309
1950-54	339	26. 0	963	74. 0	1302
Teaching Hospitals, 1945-49	83	46. 4	96	53. 6	179
1950-54	73	32. 9	149	67. 1	222

The present analysis takes into account the total stomach cancer material of the participating institutions, with the exception of:

1) Cases registered merely on the basis of death certificates; 2) cases first diagnosed at autopsy; and 3) cases who had received cancer-directed treatment before admission to a participating hospital

The first exclusion applies only to the national or State cancer registries in Connecticut, Denmark, Finland, and Norway and the third one only to the hospital materials of England and Wales, France, and the United States.

Application of these rules has led to exclusion of varying proportions of the total stomach cancer materials of the population-based cancer registries (table 2). The substantial difference between Norway and the other countries in this respect is probably due mainly to variations in the

TABLE 2.—Cancer of the stomach: number of new cases registered by population-based cancer registries during period of study, and number and percent actually included in the survival study

Country and years of diagnosis	Number of new cases registered		Included in survival study			
	Males	Females	Males	Percent	Females	Percent
Connecticut 1945-49	1437	889	985	68.5	574	64.6
Denmark 1950-54	4577	3339	3517	76.8	2098	62.8
Finland 1953-56	4494	3825	3594	80.0	2958	77.3
Norway 1953-56	3547	2452	3454	97.4	2352	95.9

handling of cases first coming to the attention of the registries through death certificates. In Norway, great efforts have always been made to obtain a full report of these cases from the doctors who signed the death certificates, as a result of which only about 2 percent of all cancer cases are registered "merely on the basis of death certificates." Without such a query program, approximately 20 percent of all cases would have to be registered on that basis. The latter figure is similar to that reported from the other countries.

The query program in Norway has shown that most of those first known from the death certificates are old persons who had not been hospitalized for cancer. With few exceptions, they have not received any tumor-directed treatment, and the diagnoses were not confirmed by microscopic examination.

The fact that a large number of such cases is included in the Norwegian material—but not to nearly the same extent as in the materials for the other countries—must be taken into consideration in the following inter-country comparisons.

*Data collection.*—The various materials included all have been compiled from pre-existing records. In other words, there has been no advance uniform planning to ensure that the admission and examination of patients, and the description of findings and treatments, would be carried out in a standardized way in all the numerous clinical departments and laboratories from which data have been collected.

Within countries, the abstracting of hospital charts and laboratory records was standardized to some extent by the request that reports to the central cancer registries be submitted on prescribed forms. However, forms as well as reporting and registration procedures have varied considerably between countries (table 2).

In the final stage, a high degree of uniformity was attained between, as well as within, countries in the classification and processing of the information as recorded by the central registries. Uniform definitions were adopted, a uniform punch card code was used by all countries, and computations and tabulation of all the data were carried out by the



National Cancer Institute, U.S.A., with the exception of the French data which were processed in Paris.

*Classification.*—It can be seen that data collection had to be restricted to such items of information as are generally found in the medical records of the average hospital. Consequently, a simple classification of the material was adopted, with the attempt to distinguish between a few broad groups only. Thus, as regards *stage of the disease*, only the following categories will be considered: 1) Cases specified as localized; 2) not localized; and 3) stage unknown.

In this context *localized* is the designation for neoplasms that were reported to be confined to the site of origin—in *casu* stomach—regardless of tumor size. Classified as *not localized* are those cases for which there was reported evidence of (a) direct infiltration of neighboring organs or tissues or (b) metastases, whether regional or distant.

This stage classification takes into account all evidence available at the time of the first treatment, including any evidence derived from surgery and histologic examination. For untreated cases, stage refers to the time of diagnosis.

Classification of *treatment* originally distinguished between the following methods: surgery; radiation; surgery and radiation; chemotherapy; and no known treatment.

As the number of patients treated by methods other than surgery alone was very small in all the countries (*see* table 5), the only distinction in the survival analysis will be between “surgery only” and “no known treatment.”

For the present purpose the designation “surgery” is limited to those procedures which include removal of the part of the stomach with the tumor. Thus, neither exploratory surgery nor bypass operations, such as gastroenterostomy, have been classified as surgery. Among those procedures so classified, no attempt was made to distinguish according to the extent of the resection or according to whether or not the operation was intended to be “radical.”

## IMPORTANT CHARACTERISTICS OF THE MATERIALS

In tables 3, 4, and 5, some features that are relevant to the subsequent comparison of survival rates are shown.

### Microscopic Confirmation of the Diagnosis

The percentage with microscopic confirmation of the diagnosis varies with age, country, and years of diagnosis. Table 3 shows that the greater part of the variation according to age and country is limited to those classified as not treated by surgery. This group “all other” (table 3) is almost exclusively composed of patients classified under “no known



treatment." An unknown proportion of them had undergone bypass operations or exploratory surgery. In some, microscopic confirmation of the diagnosis was not obtained until after death.

Inclusion of varying proportions of cases first known from death certificates may explain some of the intercountry variation in confirmation among "all other," in particular over age 60.

The most unexpected observation (table 3) is the very low percent with microscopic confirmation among those treated by surgery in Denmark and France. Figures for England and Wales also are low, but show considerable increase from 1948-49 to 1952-53.

### Stage of the Disease

The only identifiable group in this material, for which one might expect the stage classification to be reasonably reliable, is the group treated by surgery. Table 4 shows the proportion of cases with

TABLE 3.—Cancer of the stomach: percent with microscopic confirmation of the diagnosis among those treated by surgery and among all others (including untreated), by sex, age, country, and years of diagnosis

Country and years of diagnosis		0-59 years			60 years and over		
		Surgery	All other	Total	Surgery	All other	Total
<b>MALES</b>							
Denmark	1950-54	66.1	32.4	58.7	62.8	20.3	41.9
England and Wales	1948-49	72.4	24.0	46.2	65.3	22.3	36.2
	1952-53	83.1	35.8	60.9	75.1	24.3	44.3
Finland	1953-56	90.9	38.8	52.8	90.1	15.8	26.7
France	1945-57	58.6	32.6	49.4	44.8	12.4	31.6
Norway	1953-56	98.2	40.2	67.8	98.2	21.5	43.8
United States							
Connecticut	1945-49	91.5	57.2	71.5	97.2	42.5	56.8
	1950-54	96.1	70.7	83.7	97.3	54.0	69.6
Central registries	1945-49	96.1	61.5	75.2	98.6	46.9	61.4
	1950-54	98.0	71.8	85.1	98.4	60.3	74.4
Teaching Hospitals							
	1945-49	97.0	67.8	83.3	97.6	45.9	68.8
	1950-54	95.3	61.0	80.4	94.2	57.5	74.7
<b>FEMALES</b>							
Denmark	1950-54	61.9	45.6	57.9	62.5	19.9	38.7
England and Wales	1948-49	74.6	28.1	48.7	69.4	20.6	35.8
	1952-53	83.9	39.8	62.6	76.4	24.1	42.5
Finland	1953-56	92.6	42.6	54.7	89.4	12.5	19.7
France	1945-57	53.1	23.1	41.5	48.6	12.1	33.2
Norway	1953-56	98.7	52.1	73.8	99.3	15.6	33.7
United States							
Connecticut	1945-49	97.2	55.8	72.7	97.5	33.1	52.5
	1950-54	98.2	69.4	80.7	98.2	46.1	65.8
Central registries	1945-49	98.9	63.7	78.8	98.1	39.2	56.4
	1950-54	99.3	72.7	84.1	99.1	53.3	69.2
Teaching Hospitals							
	1945-49	97.7	76.9	88.0	95.7	57.1	76.0
	1950-54	97.1	76.9	86.3	98.7	56.9	78.5

TABLE 4.—Cancer of the stomach: surgically treated cases according to stage, by sex, age, country, and years of diagnosis—confirmed and not confirmed

Country and years of diagnosis		0-59 years			60 years and over		
		Number of cases	Localized cases		Number of cases	Localized cases	
			Number	Per-cent		Number	Per-cent
MALES							
Denmark	1950-54	746	437	58. 6	1300	718	55. 2
England and Wales	1948-49	588	179	30. 4	547	142	25. 9
	1952-53	709	218	30. 7	865	251	29. 0
Finland	1953-56	373	226	60. 6	324	163	50. 3
France	1945-57	254	81	31. 9	245	74	30. 2
Norway	1953-56	394	140	35. 5	762	274	36. 0
United States							
Connecticut	1945-49	129	54	41. 9	177	65	36. 7
	1950-54	153	45	29. 4	261	90	34. 5
Central registries	1945-49	308	90	29. 2	488	145	29. 7
	1950-54	342	85	24. 9	640	173	27. 0
Teaching Hospi- tals	1945-49	99	20	20. 2	126	25	19. 8
	1950-54	107	17	15. 9	171	27	15. 8
FEMALES							
Denmark	1950-54	383	219	57. 2	701	395	56. 3
England and Wales	1948-49	299	89	29. 8	333	89	26. 7
	1952-53	353	123	34. 8	500	141	28. 2
Finland	1953-56	203	110	54. 2	199	108	54. 3
France	1945-57	128	39	30. 5	146	39	26. 7
Norway	1953-56	230	69	30. 0	402	150	37. 3
United States							
Connecticut	1945-49	72	21	29. 2	120	47	39. 2
	1950-54	55	13	23. 6	164	51	31. 1
Central registries	1945-49	176	48	27. 3	262	83	31. 7
	1950-54	145	30	20. 7	334	98	29. 3
Teaching Hospi- tals	1945-49	44	11	25. 0	47	9	19. 1
	1950-54	34	7	20. 6	77	17	22. 1

localized tumor. In all countries the percent with stage unknown among those treated by surgery was so small as to be negligible.

Stage, as here defined, shows little variation with age and sex, but considerable variation between countries. Exceedingly high relative frequencies of localized tumors are reported from Denmark and Finland—from 50 to 60 percent—while the figures for the other countries range between 15.8 and 41.9 percent.

The inevitable conclusion from these differences is that the attempts made to establish a uniform stage classification have been thoroughly unsuccessful. The failure is probably due mainly to the fact that the material used for the present study had already been collected by central institutions (such as a national cancer registry) when the international Ad Hoc Group on End Results was established in 1959. Standardization of procedures from then on clearly has not been able to compensate for dissimilarities of procedures before that date.

TABLE 5.—Cancer of the stomach: all cases according to treatment, by sex, age, country and, years of diagnosis

Country and years of diagnosis	0-59 years			60 years and over				
	Number of cases	Percent treated by:			Number of cases	Percent treated by:		
		Surgery	Other	No known treatment		Surgery	Other	No known treatment
MALES								
1950-54	956	78	—	22	2561	51	—	49
Denmark	1287	46	2	52	1697	32	2	66
England and Wales	1335	53	1	46	2205	39	2	59
1952-53	1384	27	5	68	2210	15	3	82
Finland	395	64	36	—	414	59	41	—
France	829	48	3	49	2625	29	1	70
Norway								
1953-56								
United States	309	42	2	56	676	26	1	73
Connecticut	300	51	2	47	726	36	1	63
1950-54	775	40	3	57	1736	28	1	71
Central registries	672	51	1	48	1730	37	2	61
1950-54	186	53	6	41	285	44	2	54
Teaching Hospitals	189	57	2	41	364	47	1	52
1950-54								
Denmark	508	75	—	25	1590	44	—	56
England and Wales	673	44	3	53	1066	31	2	67
1952-53	682	52	2	46	1424	35	1	64
Finland	841	24	8	68	2117	9	3	88
France	210	61	39	—	253	58	42	—
Norway	493	47	5	48	1859	22	1	77
1953-56								
United States	176	41	2	57	398	30	1	69
Connecticut	140	39	3	58	435	38	1	61
1950-54	410	43	3	54	899	29	1	70
Central registries	339	43	4	53	963	35	2	63
1950-54	83	53	5	42	96	49	1	50
Teaching Hospitals	73	47	2	51	149	52	1	47
1950-54								
FEMALES								
Denmark								
England and Wales								
1952-53								
Finland								
France								
Norway								
United States								
Connecticut								
1945-49								
1950-54								
Central registries								
Teaching Hospitals								



It is noteworthy that almost without exception the relative frequency of localized lesions in the various subgroups of the material from the United States is reported to be lower in 1950-54 than in 1945-49. This tendency could be due to, for example, changes in the selection of patients with stomach cancer for admission to participating hospitals, changes in recording of findings and registration of cases, a greater tendency in recent years to operate on the more advanced cases (the percent treated surgically has increased), or to increasing thoroughness in the histopathological examination of tissue removed by the surgeon.

### Treatment

Treatment, as here defined, has almost exclusively been surgical (table 5). Most of the few cases classified under "Other" treatment received radiation alone. Only exceptionally have surgery and radiation been given in combination.

The contrasts between countries as regards percentage treated by surgery are striking. Among males under age of 60, Denmark (78%) and Finland (27%) represent the extremes, with the most recent figures for all other areas ranging from 48 to 68 percent. The corresponding figures for females are similar.

Over age 60 the percentage treated by surgery is generally smaller, but the pattern is essentially the same as in the younger age group, although among females the figures for Denmark vary less than those for some of the other countries. The highest figures are those for France (58%).

The data in table 5 reflect differences in patient selection as well as differences in treatment policies and treatment standards. An important question suggested by the data is whether the recorded contrasts may not, to some extent, be ascribable to dissimilarities in the classification of cases according to treatment. The percentage reported to have been treated by surgery in Denmark and France is exceedingly high.

In the oldest age groups much of the difference between the figures for Denmark and, for example, Norway might be due to the selection mentioned (table 2), but the difference among those under 60 in no way can be accounted for on that basis.

In those areas for which figures are broken down into two time intervals, the percentage treated by surgery is generally higher in the more recent period.

## SURVIVAL EXPERIENCE

In all countries the statistical follow-up of the patients has been very complete. The percentage of patients lost to follow-up during the first



TABLE 6.—Cancer of the stomach: corrected survival rate, by sex, age, country, and years of diagnosis—total material

Country and years of diagnosis	0-59 years				60 years and over			
	Number of cases	Corrected survival rates (%)			Number of cases	Corrected survival rates (%)		
		1 year	2 years	5 years		1 year	2 years	5 years
MALES								
Denmark	956	33.4	22.6	14.0	2561	24.1	15.3	10.6
England and Wales	1287	22.2	12.6	7.1	1697	14.4	8.3	4.3
Finland	1335	24.7	15.2	8.8	2205	18.0	10.8	6.3
France	1384	31.3	19.0	10.3	2210	19.4	9.3	5.2
Norway	395	38.0	23.4	15.6	414	33.3	19.1	11.4
United States	829	35.8	21.8	13.4	2625	23.7	13.8	7.5
Connecticut	309	29.6	19.4	11.6	676	16.4	10.3	7.4
Central registries	300	37.7	25.5	16.6	726	27.6	18.7	10.3
Teaching Hospitals	775	28.9	18.4	11.2	1736	20.2	12.3	8.2
	672	36.7	25.3	15.9	1730	29.1	18.0	9.9
	186	31.9	18.4	11.1	285	26.9	14.2	8.9
	189	31.9	21.4	12.7	364	24.9	14.6	9.5
FEMALES								
Denmark	508	34.0	22.7	12.6	1590	24.4	16.6	11.9
England and Wales	673	21.5	12.1	7.6	1066	15.0	7.4	4.1
Finland	682	23.8	14.4	7.3	1424	17.9	10.6	6.5
France	841	28.9	14.8	8.1	2117	17.5	9.2	5.6
Norway	210	45.5	34.2	19.9	253	39.6	27.4	17.4
United States	493	38.3	20.8	12.5	1859	22.2	13.5	8.8
Connecticut	176	25.1	15.0	4.7	398	23.9	14.5	9.2
Central registries	140	29.4	19.3	8.7	435	29.0	17.8	11.6
Teaching Hospitals	410	31.2	19.3	8.3	899	25.3	16.2	10.6
	339	29.6	20.0	10.2	963	28.4	18.3	11.6
	83	37.1	22.4	10.2	96	32.6	21.0	14.6
	73	35.8	13.8	4.2	149	28.6	22.6	14.3

5 years was less than approximately 1 percent and only in one of the series presented as high as 2 percent.

Survival will be expressed in terms of the *corrected survival rate*, that is, the survival rate actually observed divided by the expected survival rate, the latter derived from the appropriate national life tables.

Although 10-year survival rates are available for all countries except Finland and Norway, rates beyond the 5th year will not be presented. As a result of the excessive risk of death from stomach cancer during the first years after diagnosis, the number of cases under observation is rapidly reduced, so that even the annual survival rate for the 5th year has, in many instances, to be based on a rather small number of cases.

### Total Material

Table 6 shows the corrected survival rates for the total material, confirmed and not confirmed, treated and untreated. When only cases diagnosed in the 1950's are considered, the 5-year rates for males under age 60 range between 8.8 and 16.6 percent, and for males over that age between 5.2 and 11.4 percent. Rates are consistently somewhat lower among the older than among the younger males.

Five-year survival rates among females show greater variation, the range in the younger and older age group being 4.2 to 19.9 and 5.6 to 17.4 percent, respectively. In both age groups the highest rates are those for France. The United States data show consistently higher rates among the older than among the younger females, while the opposite is found in most European countries. Overall, the differences are slight, however, and the pattern might be due to random variation.

Age comparison shows that the males enjoy more favorable survival rates under age 60, while the females are generally at a relative advantage above that age. But again the differences are slight.

Data from Connecticut and England and Wales suggest that the cases diagnosed in the early 1950's have fared better than those diagnosed in the late 1940's. For male patients in Connecticut, the increase in the probability of surviving the first year after diagnosis is notable.

However, irrespective of the variations that were pointed out, the essential feature in table 6 is the extremely grave prognosis manifested in every group.

### Cases Treated by Surgery

In striking contrast to the foregoing data, table 7 identifies one group of patients with stomach cancer for whom the survival experience has been quite favorable, *i.e.*, those who were treated by surgery for a tumor classified as *localized*. It is true that this group constitutes a small percentage (tables 4 and 5) of the total stomach cancer group, but table 7 nevertheless demonstrates, for example, that in Norway during the 4 years

TABLE 7.—Cancer of the stomach: corrected survival rate among patients treated by surgery, by sex, age, country, and years of diagnosis—localized cases, with and without microscopic confirmation of the diagnosis

Country and years of diagnosis	Number of cases	0-59 years Corrected survival rates (%)			Number of cases	60 years and over Corrected survival rates (%)		
		1 year	2 years	5 years		1 year	2 years	5 years
MALES								
Denmark	437	57.4	40.4	25.4	718	49.4	33.3	20.5
England and Wales	179	69.9	46.2	29.9	142	52.4	38.1	19.5
1952-53	218	59.8	49.7	31.8	251	54.8	40.5	24.9
Finland	226	77.1	58.9	35.6	163	74.5	53.6	32.1
France	69	70.9	52.0	33.2	62	63.1	46.5	29.1
Norway	140	84.7	63.3	48.7	274	80.5	64.0	44.3
United States								
Connecticut	54	75.0	62.5	36.1	65	61.3	44.1	38.3
1950-54	45	78.5	63.0	48.1	90	66.7	57.8	44.5
Central registries	90	79.7	70.0	48.7	145	67.8	51.4	40.2
1945-49	85	84.3	70.3	52.1	173	72.5	63.6	49.1
1950-54	20	81.0	61.6	(43.1)*	25	71.2	57.2	(52.2)
Teaching Hospitals	17	—	—	—	27	61.2	51.5	(50.9)
FEMALES								
Denmark	219	58.3	42.0	23.2	395	51.6	38.7	25.4
England and Wales	89	67.8	49.9	36.8	89	47.5	31.2	19.1
1948-49	123	55.6	37.8	21.9	141	64.0	48.3	34.6
1952-53	110	75.7	53.6	32.7	108	71.2	61.2	32.2
Finland	33	72.0	58.8	32.9	34	52.4	38.7	27.9
France	69	94.6	70.2	44.4	150	82.1	73.2	59.7
Norway								
1953-56								
United States								
Connecticut	21	62.3	48.3	(14.9)	47	64.2	50.8	42.5
1945-49	13	92.8	77.2	(26.4)	51	67.6	57.8	48.4
1950-54	48	73.3	59.1	28.1	83	67.1	51.0	44.5
Central registries	30	93.9	84.2	50.3	98	77.3	61.6	48.3
1950-54	11	—	—	—	9	—	—	—
1945-49	7	—	—	—	17	—	—	—
Teaching Hospitals								
1950-54								

\*Figures in parentheses indicate annual rate based on less than 10 cases.



1953-56 no less than 633 such cases were registered, with a 5-year corrected survival rate close to 50 percent.

Table 7 shows that the 5-year survival rate, almost without exception, has been somewhat better among younger than among older males, but no definite pattern is observed among the females. The data for England and Wales and the United States indicate slightly higher 5-year rates for patients from the more recent calendar period.

The most conspicuous finding (table 7) is the difference in 5-year survival rates between those of Denmark, England and Wales, Finland, and France and those of Norway and the United States. Thus, considering only the most recent figures, the rates for males under age 60 in the first group of countries range from 25.4 to 35.6 as compared with 48.1 to 52.1 for the latter group. The picture is essentially the same when cases without microscopic confirmation of the diagnosis are excluded.

The relatively low 5-year rates for Denmark and Finland could easily be due to lack of conformity of the criteria used for classifying cases according to stage. As previously indicated, when compared with the other countries both Denmark and Finland have an unreasonably large proportion of their surgical cases classified as localized, which clearly means that in those two countries the proportion that was erroneously so classified was even higher than in the other countries.

The relatively low survival rates observed in the material from England and Wales and France are more difficult to explain on the basis of the available data. The high probability of death during the first year after diagnosis in England and Wales would seem to be compatible with an explanation similar to that for Denmark and Finland, but the proportion of cases classified as localized in England and Wales is not particularly high, as seen in table 4.

In Norway, special efforts were made to determine accurately the stage of those cases in which, according to the routine notifications, no metastases had been demonstrated during operation or in the surgical specimen. For all these cases the pathology reports were reviewed for possible evidence of direct tumor infiltration of neighboring tissues or organs. Cases in which such infiltration had been demonstrated were classified as not localized. As far as is known, no review of this kind has been undertaken in the other European countries. It is possible, therefore, that the designation "localized" has been used in a stricter sense in Norway, and this could provide a partial explanation for the relatively favorable survival rates for that country. It is notable, however, that the proportion of the surgical cases that has been classified as localized is fairly high in the Norwegian material.

The survival experience of those classified as *not localized* is shown in table 8. Again the 5-year rates for Denmark and England and Wales



TABLE 8.—Cancer of the stomach: corrected survival rate among patients treated by surgery, by sex, age, country, and years of diagnosis—cases classified as not localized, with and without microscopic confirmation of the diagnosis

Country and years of diagnosis	Number of cases	Corrected survival rates (%)			Number of cases	60 years and over Corrected survival rates (%)			
		1 year	2 years	5 years		1 year	2 years	5 years	
MALES									
Denmark	1950-54	309	9.1	4.6	(1.7)*	582	10.0	4.3	3.2
England and Wales	1948-49	409	30.0	16.8	8.5	405	25.1	14.6	8.4
	1952-53	491	32.2	15.8	8.2	614	28.4	17.0	10.5
Finland	1953-56	138	60.7	33.5	16.7	154	51.2	25.6	16.8
France	1945-57	173	29.8	15.7	10.8	171	20.2	7.8	5.0
Norway	1953-56	246	52.4	26.4	11.2	458	45.4	24.2	9.3
United States									
Connecticut	1945-49	67	45.3	26.0	17.7	104	22.8	16.3	8.7
	1950-54	96	52.7	30.8	17.7	159	48.9	31.4	14.7
Central registries	1945-49	200	47.6	25.1	12.4	330	36.6	21.1	11.9
	1950-54	235	50.6	33.6	18.7	446	50.7	29.9	13.6
Teaching Hospitals	1945-49	78	40.2	19.7	(9.6)	100	41.8	17.5	(9.0)
	1950-54	87	38.4	23.5	8.6	140	38.4	22.3	9.3
FEMALES									
Denmark	1950-54	164	15.9	8.0	(4.4)	306	14.9	5.6	3.7
England and Wales	1948-49	210	30.6	13.9	7.3	244	25.7	13.1	6.6
	1950-54	230	34.9	19.3	9.0	359	29.9	16.3	8.2
Finland	1953-56	90	57.0	32.6	17.0	90	46.0	23.9	15.2
France	1945-57	89	34.4	22.9	14.7	107	30.2	20.9	13.6
Norway	1953-56	155	55.0	26.7	13.1	246	53.4	28.0	13.1
United States									
Connecticut	1945-49	47	40.6	25.8	(6.6)	72	50.3	28.3	18.6
	1950-54	40	47.8	32.5	(16.7)	109	42.1	25.1	12.9
Central registries	1945-49	122	48.0	27.6	9.1	173	49.9	29.1	16.9
	1950-54	110	43.9	26.5	9.5	229	46.3	28.8	14.3
Teaching Hospitals	1945-49	33	45.6	21.4	(6.2)	38	46.1	30.8	(22.1)
	1950-54	27	55.8	26.2	(7.6)	60	39.9	28.9	(12.3)

\* Figures in parentheses indicate annual rate based on less than 10 cases.

are lowest, but now the Finnish rates are among the most favorable recorded.

The most reasonable explanation for the low Danish survival rates seems to be that the group "treated by surgery, not localized" in Denmark is loaded with more advanced cases, due to a selective transfer of the less-advanced cases to the "localized" group, as previously suggested. Furthermore, since an exceptionally large proportion of the total Danish group is reported to have been treated by surgery, it is conceivable that the definition of surgery actually used in classifying the Danish cases may have been more comprehensive than the somewhat narrow definition formally adopted by the End Results Group. This would probably mean that bypass operations are included, and since this surgical procedure is mostly reserved for the advanced, nonresectable cases, the effect would again be to load the Danish group "treated by surgery, not localized" with desolate cases.

Differences in the criteria used in the classification of cases according to stage and treatment may, in a similar way, have affected the survival figures for England and Wales. However, as far as the available data are concerned, there is admittedly nothing but the relatively low survival rates to support such an assumption.

#### Untreated Cases

To complete the picture the corrected survival rates for those receiving no known treatment are shown in tables 9 and 10. It was believed that the most relevant distinction within this very large group would be according to whether the diagnosis had been microscopically confirmed, and this distinction is what the two tables demonstrate.

The majority of the confirmed cases (table 9) were specified as not localized. The clinical characteristics of this group are reflected in the 1-year survival rates, most of which are less than 10 percent. There is an occasional 5-year survivor. An unknown percentage of the patients in this group had undergone anastomosing operations.

Those cases without microscopic confirmation of the diagnosis (table 10) are very heterogeneous with regard to stage distribution. Understandably, in some countries a large proportion of these cases has been classified under "stage unknown." In the Danish material all the cases have been classified as not localized. At first sight it was somewhat surprising, therefore, to find that the corrected 5-year survival rate for Denmark is about 10 percent. Obviously this means that some of the cases—presumably about 10 percent of the total group—had not, in fact, been cases of stomach cancer. Very high rates are also reported for some of the French groups. Thus, among 45 female patients under age 60, the corrected 5-year survival rate is stated to be 36 percent.

TABLE 9.—Cancer of the stomach: corrected survival rate among patients with no known treatment, by sex, age, country, and years of diagnosis—microscopically confirmed cases only

Country and years of diagnosis	0-59 years			60 years and over					
	Number of cases	Corrected survival rates (%)			Number of cases	Corrected survival rates (%)			
		1 year	2 years	5 years		1 year	2 years	5 years	
MALES									
Denmark	1950-54	68	16.3	5.9	(1.5)*	256	9.1	5.3	(2.8)
England and Wales	1948-49	149	0.6	0		246	2.3	(1.0)	0
	1952-53	213	4.7	1.9	(1.0)	312	3.7	0.7	(0.4)
Finland	1953-56	347	14.0	5.1	(1.6)	271	14.4	2.9	(1.0)
France	1945-54	<30	—	—	—	<30	—	—	—
Norway	1953-56	157	8.9	4.5	(1.3)	379	5.5	1.4	(0.6)
United States	1945-49	100	7.6	(2.2)	0	207	5.6	1.6	(0.6)
Connecticut	1950-54	100	10.8	(6.0)	(1.2)	248	7.9	2.6	(0.6)
Central registries	1945-49	272	7.1	2.0	(0.4)	574	5.4	2.3	(0.9)
	1950-54	228	9.6	4.3	(1.1)	639	8.7	2.8	(0.4)
Teaching Hospitals	1945-49	51	3.9	(2.0)	(2.1)	70	2.9	0	
	1950-54	47	12.9	(4.3)	(4.6)	108	4.8	(1.0)	(1.2)
FEMALES									
Denmark	1950-54	57	12.3	(8.8)	(5.4)	177	5.4	(1.9)	0
England and Wales	1948-49	89	1.1	(1.1)	0	143	1.4	0	
	1952-53	123	2.4	(0.8)	0	216	2.9	0	
Finland	1953-56	223	16.6	4.5	0	214	13.1	6.1	(4.6)
France	1945-57	<30	—	—	—	<30	—	—	—
Norway	1953-56	118	5.9	(0.8)	0	215	5.8	1.0	0
United States	1945-49	57	1.7	0		92	5.7	(2.3)	0
Connecticut	1950-54	56	5.3	(1.8)	(1.8)	123	9.3	1.7	0
Central registries	1945-49	141	6.8	(1.7)	(0.8)	244	6.0	2.7	0
	1950-54	130	7.0	(2.6)	(1.8)	323	10.1	3.1	(1.6)
Teaching Hospitals	1945-49	28	10.7	(3.6)	0	27	7.6	(3.9)	(4.5)
	1950-54	28	10.7	0		40	0		

\* Figures in parentheses indicate annual rate based on less than 10 cases.

TABLE 10.—Cancer of the stomach: corrected survival rate among patients with no known treatment, by sex, age, country, and years of diagnosis—unconfirmed cases only

Country and years of diagnosis	0-59 years				60 years and over			
	Number of cases	Corrected survival rates (%)			Number of cases	Corrected survival rates (%)		
		1 year	2 years	5 years		1 year	2 years	5 years
MALES								
Denmark 1950-54	142	20.5	15.0	11.8	1005	17.7	10.9	9.3
England and Wales 1948-49	517	5.6	1.0	(0.2)*	875	6.5	2.3	(1.0)
1952-53	395	6.7	2.6	(0.7)	990	6.6	2.1	(0.4)
Finland 1953-56	601	14.8	7.5	4.0	1546	10.6	3.9	1.7
France 1945-57	64	37.6	28.0	11.5	109	38.2	10.1	0
Norway 1953-56	251	8.2	3.7	(3.0)	1453	9.5	2.9	0.7
United States								
Connecticut 1945-49	72	7.8	(3.1)	0	285	10.9	5.6	(3.5)
1950-54	42	16.8	(9.7)	(7.7)	209	15.0	7.9	(1.5)
Central registries 1945-49	172	12.3	6.6	(7.0)	652	13.5	7.5	4.9
1950-54	92	18.7	7.8	(7.0)	423	17.1	7.5	(2.2)
Teaching Hospitals 1945-49	25	22.7	(13.8)	(14.7)	84	16.5	8.7	(1.7)
1950-54	31	14.9	(7.6)	(4.0)	80	16.3	8.7	(8.6)
FEMALES								
Denmark 1950-54	68	17.7	7.4	(4.5)	712	17.6	12.2	10.1
England and Wales 1948-49	265	4.9	1.9	(0.7)	574	8.4	2.6	(1.2)
1952-53	193	5.7	3.1	(1.0)	694	6.7	2.9	(1.5)
Finland 1953-56	347	12.6	3.5	(2.4)	1645	11.8	4.4	2.8
France 1945-57	45	57.8	34.9	36.0	73	34.0	14.2	0
Norway 1953-56	120	12.5	6.7	(5.1)	1228	10.7	4.6	1.7
United States								
Connecticut 1945-49	44	18.3	(2.3)	(2.3)	182	12.2	5.6	(0.8)
1950-54	25	20.1	(8.1)	(4.1)	144	21.5	11.1	(7.0)
Central registries 1945-49	81	22.6	9.4	(6.5)	381	17.2	11.4	6.1
1950-54	50	19.3	(10.8)	(6.1)	289	17.8	11.2	6.4
Teaching Hospitals 1945-49	7	(23.2)	0	0	21	12.7	0	(1.7)
1950-54	9	(33.6)	(11.3)	0	31	27.2	(21.7)	(13.1)

\* Figures in parentheses indicate annual rate based on less than 10 cases.



## CONCLUDING REMARKS

The study reported here is part of the comprehensive survival studies carried out by the International Ad Hoc Group on End Results of Cancer Treatment. The purpose of these studies has been to establish, by standardized methodology, survival rates for several forms of cancer, in a number of countries, and to compare the rates with a special view to the possible influence of treatment on survival.

It should be clearly understood that the work now completed by the Ad Hoc Group has been exploratory in nature. The most that could be hoped for was that these studies would lead to the recognition of problems which could subsequently be pursued in properly planned studies.

The stomach cancer study agrees with many previous studies in showing that in general the prognosis for patients with this form of cancer is extremely poor. Yet, for patients treated by surgery—as here defined—for a localized tumor, the corrected 5-year survival rate is close to 50 percent in some countries.

Some striking international differences in survival rates for stomach cancer have been observed. This pertains in particular to patients treated by surgery. But it seems that differences in the selection of patients and differences in the criteria used for classification of cases according to stage and treatment may easily account for the observed difference in survival.



**Surgery for Gastric Cancer at the University  
of Minnesota Medical Center, 1936 Through  
June 30, 1958<sup>1</sup>**

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**I. CLINICAL DISCUSSION**

**G**ASTRIC cancer appears to be on the decline in our country. Many continue to ask, "Why is not the accomplishment in gastric cancer better?" In 1956, the suggestion was made that more than 20 percent of all patients with gastric cancer seen in clinics with a real interest in the problem might be salvaged by surgery a decade hence (1). Experience is chastening. Despite the long, continued interest in gastric cancer in this clinic, the 15 percent survival (2), reported for the years 1950-53 for all patients with gastric cancer seen in the clinic, has not been exceeded—in fact, has not been equaled again. The 5-year survival rate for all 1,756 patients with gastric cancer seen at the University Medical Center over the 22½ years from January 1, 1936, to June 30, 1958, is 10.4 percent; the age-adjusted 5-year survival rate is 13.1 percent. Only early recognition of mucosal gastric cancer apparently will make it possible to salvage 25 percent of all patients with gastric cancer.

**Likely Reasons for Poor Achievement in Gastric Cancer**

The factors accounting primarily for the poor results of surgery for gastric cancer are: 1) the long asymptomatic, latent period—on the average 20 months—between the presence of cancer that is identifiable

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histologically and symptoms; 2) presence of cancer in the regional lymph nodes; 3) extension of the cancer, when diagnosed, to the serosal surface of the stomach; and 4) the high potential malignancy of a large proportion of gastric cancers.

### Problems of Recognition

Conventionally in our experience, 4 to 6 months are lost between the time the patient first experiences symptoms and the time he consults a physician and a somewhat similar period before a decisive diagnosis is made. This time-loss period has not changed materially in this clinic over the past 20 years. However much we lament this occurrence, the more important consideration is the circumstance that all patients with visceral cancer probably have a long asymptomatic period, which in gastric cancer appears to range between 18 and 27 months (3, 4). This circumstance suggests the need of subjecting patients in age groups in which gastric cancer may be frequent to periodic scrutiny (5). Our own experience on this score with available techniques of examination in the Cancer Detection Center has been disappointing (6). Cancer detection has proved extremely helpful and useful in cancer of the cervix, of the uterus, the rectum, and the breast, as will be pointed out in another part of this program.

The relatively asymptomatic course of gastric cancer until the lesion is fairly well advanced is well expressed by Theodor Storm in his poem entitled, "Beginn des Endes." Storm died of a gastric cancer in 1888, several years before Roentgen's great discovery came to have frequent application in abdominal diagnosis.

'Tis but a prick, 'tis scarce a pain,  
Just felt, to which no name you give:  
Henceforth it speaks again—again,  
Uneasy now you have to live.

If to complain you try—of what?  
You cannot put it into speech:  
Within you say, "Indeed 'tis naught!"  
Henceforth it holds fast like a leech.

So seldom strange your world does grow,  
And quickly are you stript of hope,  
Until at last you really know  
That with Death's shaft you cannot cope.

In effect, in these three short stanzas, Storm, suffering with his gastric cancer says: "1) I have a pain. 2) Oh, it is nothing. 3) It is too late." Even today, this typifies the sequence in too many patients who have gastric cancer.



For the stomach, radiography is still the most important agent in the earliest possible detection of gastric cancer. We have interpolated histamine achlorhydria as a screening test to determine which patients should be submitted to roentgenologic study. Yet, experience has taught that with the use of current roentgenologic techniques mucosal gastric cancer is not recognized. Only when the musculature of the gastric wall is invaded are roentgenologists able to make the diagnosis with regularity. Development of a technique for the identification of gastric mucosal cancers, while the lesion is still limited to the mucosa, would make a significant impact upon the results of gastric cancer surgery.

### Surgical Management of Gastric Cancer

As modest as the accomplishment of surgical therapy in gastric cancer is, it cannot be denied it is still superior to any other available form of therapy. That gastric cancer is on the decline suggests definitely there must be external or environmental factors which affect the situation, perhaps no more readily understood than is the early detection of gastric cancer. It is the belief of surgeons at the University of Minnesota that persistent, relentless efforts directed at development of new techniques for recognition of silent, asymptomatic gastric cancer offer the best hope of improving the results. A few years ago, a report was made on the use of radioactive phosphorus, employing photosensitive inlying gastric balloons, in the recognition of gastric cancer (7, 8). Unfortunately, the disparity of affinity for radioactive phosphorus between the malignant tissue and the normal contiguous tissue is not great. Yet, these small differences augmented by the element of time, with a photosensitive inlying gastric balloon in place for 2 to 4 hours, permit recognition of gastric cancers by this technique. Moreover, difficulties relating to impregnation of latex with photosensitive substances have been experienced by the Eastman Kodak Company, which prepared these balloons for us. Currently, we are experimenting with balloons made of a single chemical substance in the hope that some of the prior difficulties will be eliminated; latex, after all, is far from being a chemically pure substance.

Professor Friedrich of Heidelberg (1874) reported that he cured a patient with gastric cancer by the administration of Decoction of Condurango (9). However, this was 20 years before Conrad Roentgen's important discovery and an additional 20 years were to elapse before roentgen rays came to be used frequently for the recognition of gastric cancer. In my years as a medical student directly after World War I, an internist in our outpatient clinic sent patients home when the diagnosis of gastric cancer was established, believing that surgery had nothing to offer. He gave these patients a prescription for Decoction of Condurango, much as Friedrich had done long years earlier. Undoubtedly, in Fried-

rich's case, the patient must have had a benign gastric ulcer, an error in diagnosis which is made more than occasionally even today. While we all decry the fact that the results of surgery for gastric cancer are not better, there are few complete therapeutic nihilists abroad today. However, one does encounter them occasionally, as at a discussion on gastric cancer (10) held in the Walter Reed General Hospital less than 10 years ago.

### Regional Lymph Nodes

That patients with gastric cancer and cancer-free lymph nodes at operation achieve a cure rate far surpassing those with lymph-node-positive cancers should encourage routine performance of a radical procedure in standard-risk patients. The second-look procedure has contributed importantly to elaboration of an adequate operation for gastric cancer. It is important, obviously, to completely excise the cancer in the organ from which it originates. Were total gastrectomy a simpler operation and unaccompanied by any untoward effect, total gastrectomy certainly would be the operation of choice for most, if not all, gastric cancers. However, this procedure is probably mandatory only in instances of linitis plastica, in diffuse mucosal cancers, extensive cancers involving the greater portion of the stomach, and for cancers high on the lesser curvature of the stomach. An equally important desideratum is excision of the lymph node drainage area. It is here the second-look procedure has been valuable in indicating where residuals may be found after what otherwise was believed to be a complete operation (11). These studies have shown that not only is excision of the lesion in the stomach and juxtagastric-lying nodes mandatory, but that it is equally as important to remove the lymph nodes along the entire extent of the hepatic artery.<sup>2</sup> This is especially true in antral lesions in which we have come to perform complete dissection of the lymphatic tissue surrounding the hepatic pedicle in all standard-risk patients. It is a bit dismaying to see a surgeon professing a lively interest in the surgery of gastric cancer content himself with excision of the gastric lesion and the lymph nodes in the gastrohepatic omentum and sacrificing also the greater omentum, believing that such a procedure constitutes complete operation for gastric cancer. Many gastric surgeons have come to feel that splenectomy, as well as the extensive lymph node dissection described herein, should be a part of the conventional operation for gastric cancer in the standard-risk patient.

After excision of the stomach and dissection of the lymph nodes as described, it is important to remove lymph nodes along the superior border of the pancreas as well. In such dissections for high-lying gastric cancers, it is important to look carefully for and to excise lymph nodes about the tail of the pancreas. If there is invasion or direct adherence between the

<sup>2</sup> This portion of the dissection was carried out quite regularly before Arhelger's important work (11) pointed out the necessity for the hepatic pedicle dissection in antral cancers.

pancreas and the posterior wall of the stomach, it is obviously in order to sacrifice the distal portion of the pancreas. Extensive involvement of the transverse mesocolon or adherence of cancer of the greater curvature to the transverse colon may necessitate sacrifice of a segment of the transverse colon. When the lymph nodes are involved, those most difficult to excise are along the greater curvature of the stomach in the pyloroduodenal area.

Whereas there have been more limited series of cases in this clinic in which the operative mortality for the extended lymph node dissection as a regular accompaniment of gastric resection for cancer has been less than 5 percent, as the tables indicate, the over-all mortality over a long period is considerably higher (tables 2 and 3).

However, if one could maintain the mortality for operations for gastric cancer under 5 percent, even so, such an accomplishment could not compete with the virtue and promise of early diagnosis before lymph nodes become involved.

TABLE 1.—Cancer of the stomach, 1950–1958

	Number of cases	
Operations*	537	
Resections†		431
Curative		268
Palliative		163
Not resected		106
No surgery	67	
All cases	604	

\*Operative rate = 89 percent.

†Resection rate = 80 percent.

TABLE 2.—Operative mortality—Cancer of the stomach, 1950–1958

	Curative			Palliative		
	Num- ber of cases	Operative deaths		Num- ber of cases	Operative deaths	
		Num- ber	Per- cent		Num- ber	Per- cent
Partial gastrectomies	166	22	13	96	23	24
Total gastrectomies	102	23	22.5	67	25	37

TABLE 3.—Cancer of the stomach—Resections for cure, 1950 through June, 1958

	Number of cases	5-year survivors		Operative deaths	
		Number	Percent	Number	Percent
+ Nodes	158	28	18	25	16
– Nodes	110	46	42	20	18
All cases	268	74	28	45	17



There are undoubtedly therapeutic nihilists who would have us believe there is no relationship between duration of symptoms and extent of lymph node involvement, that the difference in prognosis is due solely to the initial malignancy of the disease. However, most observers go along with the thesis that for most malignancies, there usually is a time relationship between the duration of the cancer and the absence or presence of lymph node metastasis (12).

## II. SURVIVAL DATA

Available information 20 or 30 years ago, including mortality and incidence figures and scientific reports in the medical literature, appeared to indicate a continuing increase in gastric cancer. However, subsequent events have demonstrated that reported incidence rates for cancer of the stomach in the United States have declined significantly over the past decade, and more precise definition remains to be made concerning the causative factors involved. Cancer of the stomach, nonetheless, continues to account for a significant number of the deaths from malignant disease in the United States and is responsible for an even greater proportion in other areas of the world, especially in Iceland, Finland, and Japan.

At the University of Minnesota Hospitals, 1,756 patients with stomach cancer were seen between 1936 and June, 1958, a period of 22½ years during which 5-year survival could be ascertained (table 4). For all the 1,756 patients, we have had a 100 percent follow-up for at least 5 years; 4 of these patients have now survived for more than 20 years. A total of 183 patients have survived 5 years or longer, for an over-all "crude" survival rate of 10 percent or an age-adjusted rate for the 22½ years of observation of 13 percent.

Particular attention was directed to the patients seen between 1950 and June, 1958, the relatively recent group for which 5-year follow-up studies could be made. The over-all "all cases-all stages-confirmed and not confirmed" group is comprised of 604 patients. Again, as with cancer of the rectum and colon, the percentage of cases "not confirmed" was less than 10 percent. The "crude" 5-year survival rate for the over-all group was 12 percent. The age-adjusted survival rate for this group was

TABLE 4.—Cancer of the stomach (all cases) 1936 through June, 1958

	Number of cases	5-year survivors	
		Number	Percent
1936-1941	328	22	6.7
1942-1949	824	87	10.6
1950-1953	327	48	14.7
1954-1958	277	26	9.4
Over-all	1,756	183	10.4



15 percent. When only the confirmed cases are considered, this over-all 5-year survival rate was 14 percent and the age-adjusted survival rate was 17 percent.

During the period 1950-58 at our institution, 110 "confirmed," localized cases were treated surgically. Of these 110 patients, 46 survived 5 years or more for an age-adjusted survival rate of 55 percent, a rate that equals that of other reporting registries. However, a comparison of the results following all surgical excisions performed (both curative and palliative) showed that the rate of survival of the University of Minnesota patients was quite low. This is accounted for by the fact that whereas the excision rate for all patients seen during this period was 71 percent, 40 percent of these excisions were "palliative" (13-16).

### SUMMARY

The experience and modest accomplishment of a university clinic in the management of gastric cancer are summarized over a period of 22½ years. The over-all 5-year survival rate for this period was 10.4 percent and did not improve during the last period of study, 1954-58. In Minnesota since World War II, a higher proportion of late cases appear to be coming to the University of Minnesota Medical Center. The over-all admissions for gastric cancer were fewer, occasioned in part by a decline in the observed frequency of the disease, but an even more important circumstance is that an increasing number of hospitals throughout the state have well-trained surgeons who are beginning to wrestle with the problem.

It appears that only development of techniques that will permit early recognition of gastric cancer will succeed in improving the results of surgical therapy.

As noted also in the treatment of patients with bowel cancers, an increased proportion of patients with gastric cancer subjected to excisional procedures appears to indicate an over-all improved prognosis: 1) improvement in the efficacy of the therapy itself; 2) palliation by virtue of excision of the primary neoplasm, noticeably apparent in the gastric second-look failure group; and 3) focusing public attention upon the problem, thus promoting public awareness of the virtues of earlier diagnosis and more adequate therapy.

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## **The Second-Look Operation for Abdominal Malignancies, 1948-1963<sup>1</sup>**

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**R**EGIONAL lymph node involvement in cancer decreases curability attending surgical excision. Experience teaches that the silent interval in gastric cancer is about 20 months. It is likely that the same interval between histological appearance or evidence of cancer and the assertion of clinical symptoms, for most visceral cancers, parallels that of gastric cancer. It is this observation that prompted the second-look program, as an attack on lymph node positive cancers, at the University of Minnesota Medical Center in 1948 (1-4).

### **INDICATIONS FOR SECOND-LOOK PROCEDURES**

The second-look procedure has been applied in this clinic principally in patients who originally had cancers of the stomach, rectum, or colon with metastases to the regional lymph nodes. It perhaps should be employed in patients in whom the cancer extends also to the serosa. This was done in our earlier experience of 1948-52. Of 11 patients, with Dukes B colon lesions, no residual cancer was found 6 to 8 months later and this indication was abandoned. Yet, of those 11 patients 5 died of their malignancy. Retroperitoneal sarcomas (5) (rhabdomyosarcoma) and ovarian malignancies (6) also have been submitted to second-look procedures approximately 6 months after the original operation. While the patients are still asymptomatic and have

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no clinical or roentgenologic evidence of residual cancer, re-exploration is carried out in the second-look group of patients.

## THE SECOND-LOOK PROCEDURE

The entire operative field of the original procedure is carefully inspected. If any residual cancer is found, it is removed, if possible. Subsequent similar explorations are carried out at intervals of 6 months to a year in all patients in whom residual cancer is found, until no residual cancer is found or until the situation is obviously out of hand. Once the patient undergoes an exploration that reveals no residual cancer, additional operations are not recommended. However, in patients in whom at the primary operation extensive cancer is present, an additional look is advised 2 years after a negative look.

These procedures can be long and difficult. Even when no residual cancer is found, this circumstance can only be established by a painstaking scrutiny and search of the original operative region and its environs. Moreover, it is not uncommon for the pathologist to have 30 or more separately labeled specimens to examine microscopically before establishing the fact that a second-look operation is negative for cancer. Residual cancer, if present, is most likely to be found in the vicinity of the original cancer; yet, as experience has shown, it may be in unexpected locations in the abdominal cavity. In the comparatively favorable cases, the most frequent sites of residual cancers are in lymph node chains beyond the reach of the original dissection. If in a patient with colic cancer with metastases to lymph nodes, the para-aortic lymph nodes in a left-sided lesion and the paravena cava lymph nodes in a right-colon lesion were not removed at the primary operation, as they should be in a well-directed attack upon cancer of the colon in the standard risk patient, these areas are the first sites subjected to inspection and removal of the lymph nodes.

In an earlier phase of the second-look program, wide resections of portions of both lobes of the liver or excision of the right or left lobe were carried out in a number of patients for extensive hepatic metastases (7). In fact, the first successful excision of the right lobe of the liver for metastatic cancer was performed in this clinic in 1949 (8). The patient had previously undergone near-total excision of the stomach for malignancy. He survived only 7 months following right hepatic lobectomy. The only permanent cures in this clinic following hepatic resection for cancer have been from direct invasion of the liver accompanying gastric or colic cancer. Resections of other intra-abdominal viscera including pancreas, segments of small or large intestine, and portions of the diaphragmatic leaf as required by the situation for complete removal of any obvious residual cancer have been done in a



number of instances. In other words, when technically feasible and without too great apparent risk to the patient, any residual or recurrent cancer found has been removed at each subsequent operative procedure. Obviously, use of the second-look approach demands the patient be told that he has cancer (10). Moreover, we have yet to surprise a patient by imparting this information to him.

## RESULTS OF SECOND-LOOK OPERATIONS

During the 15 years the second-look program has been in operation, 226 patients who have had cancer of the stomach, colon, or rectum with metastatic lymph node involvement have had 312 "look" operations. Of the total group, 112 patients (49.5%) were found to harbor residual cancer at the first re-exploration. Seven patients who had residual cancer at their first second-look operation have come eventually to be free of evidence of cancer at a final look. All 7 of these patients were alive and well 5 years following their final look and many of them more than 10 years since their original procedure. This constitutes an over-all salvage rate of 6.2 percent of patients with hitherto hopeless residual cancer.

Two additional patients have had one positive look, but for one reason or another have failed to be explored again to establish the fact that they were free of cancer. One of these patients had a gastric resection in 1952 and a positive second-look 3 months later. Six months after the second look he was readmitted for another exploration and complained of back pain. X rays of the thoracic and lumbar spine showed bony defects and several collapsed vertebrae which were interpreted as evidence of metastatic disease. The patient did not undergo surgery but was followed in the clinic for the next 7 years. The bony lesions never changed, and he maintained good health and nutrition until he died of a myocardial infarct, circumstances which suggested the roentgen films of the spine may have been misinterpreted. The other patient, a 58-year-old lady, who underwent a combined abdominoperineal resection in 1955 for a lymph-node-positive cancer of the rectum, had a positive second look 7 months after the original surgery. She has steadfastly refused further surgery while maintaining robust health and no clinical or roentgenological evidence of recurrence. These 2 patients might therefore also be considered as conversions of the second-look procedure, under which circumstance the conversion rate would become 8.9 percent.

The palliative value of the second-look procedure has not been easy to evaluate. Tables 1, 2, and 3 show how long the patient may live before succumbing to the malignancy. Moreover, the patient's own more hopeful outlook, if he knows he has not been abandoned, has an important bearing on his well being. Palliation in the gastric cancer group was notable in

TABLE 1.—Adenocarcinoma of the stomach: postoperative survival

Group	Percent surviving				
	1 yr	2 yr	3 yr	4 yr	5 yr
Excision for cure of Dukes C lesions					
Over-all group	65	35	28	25	19
Died of recurrent cancer					
Over-all group	57	18	11	7	0
Second-look patients	84	41	25	19	3
Palliative excision	10	2	0	0	0

Reprinted from *Surgery* 51: 163-168, 1962.

that the number of patients, who were not cured and who fell therefore into the second-look failure group but who lived for more than 4 years, was 19 percent (9).

One hospital death occurred among patients who had a negative exploration for malignancy. This 64-year-old lady, whose cancer of the colon had been removed 9 months earlier, developed a cerebrovascular accident on the 2d day after a negative look and died on her 5th post-operative day. Otherwise all hospital mortality was in patients who had residual cancer at the time of their second-look procedure. Operative mortality largely was occasioned by aggressive attempts to remove large metastatic deposits in multiple organs and especially the liver. Interestingly enough, these operations concerned mostly the colon cancer group. The operative mortality based on the number of patients has been 5.6, or 3.8 percent based on the total number of look operations performed. If the patients who underwent extensive hepatectomy are excluded, the operative mortality for all operations is less than 2 percent (table 4).

TABLE 2.—Adenocarcinoma of the colon: postoperative survival

Group	Percent surviving							Median survival (months)
	6 months	1 yr	18 months	2 yr	3 yr	4 yr	5 yr	
Excision for cure of Dukes C lesions								
Over-all group	91	84	71	69	59	49	43	46
Died of recurrent cancer								
Over-all group	83	71	50	45	29	10	—	18
Second-look patients	97	88	65	38	12	6	—	21
Palliative excision	66	27		11	5	2	—	11
Colostomy only	34	15		2.5	2.5	—	—	3

Reprinted from *Surgery* 51: 163-168, 1962.

TABLE 3.—Adenocarcinoma of the rectum: postoperative survival

Group	Percent surviving									Median survival (months)
	6 months	1 yr	18 months	2 yr	3 yr	4 yr	5 yr	6 yr	7 yr	
Excision for cure of Dukes C lesions										
Over-all group	85	70	59.5	49	36	27	21	17	14.5	24
Died of recurrent cancer										
Over-all group	83	67	55.5	44	30	20	13	9	6	21
Second-look patients	100	92.5	81.5	63	37	18.5	7	4	—	26
Palliative excision	73	49		20	9	7	2	2	—	12
Colostomy only	42	21		5	2	—	—	—	—	5

Reprinted from *Surgery* 51: 163-168, 1962.

The 5-year conversion or salvage rates for the three types of cancers under discussion are 8.7 percent for colon cancer, 5.3 percent for stomach cancer, and 3.6 percent for rectal cancer. The colon group is the most heartening, and it is the one in which we have continued aggressive surgical efforts at conversion to a negative cancer status. The rectal cancer group is disappointing, not only because of the low salvage rate but also because of the high failure rate. The *sine qua non* of all surgical efforts directed at the extirpation of cancer is an adequate primary cancer operation. As every surgeon comes to know, this is difficult to achieve in the patient with a low-lying rectal cancer extending through the bowel wall.

### COMMENT

The achievement of the second-look program leaves much to be desired. The learning process has been slow. Some of our negative-look patients who subsequently died of cancer had their first re-exploration too early. The extent of the cancer at the primary operation should have some influence on when the first relook is undertaken. If only a few lymph nodes

TABLE 4.—Second-look results: operative mortality

Number	Percent
226 patients	5.6
312 operations	3.8
300 operations (excluding hepatectomies)	1.8

TABLE 5.—Second-look results in retroperitoneal sarcomas (rhabdomyosarcoma)

Status	Number of patients
Living and well; last look, negative (months survival since negative operations 180, 156)	2
Living and well, last look, positive	1
Dead of sarcoma (48, 108, 132, and 132 months after diagnosis made)	4
Operative death	1

are involved and if the lesion comes to the peritoneal surface in only a small area, re-exploration a year after the initial primary operation is probably in order. For patients with considerable cancer at the first operation, a first look at 6 months should be done.

Our experience with second-look procedures for large retroperitoneal rhabdomyosarcomas (table 5) and for ovarian malignancies with relatively low mortality and morbidity (tables 6 and 7) has been good.

The second-look program has been helpful in emphasizing the modes of spread of certain visceral malignancies. The hepatic artery and porta hepatis dissection as a component of the complete operation for gastric cancer grew essentially out of experiences with the second-look procedure. Also, routine use of para-aortic and paracaval node dissections for colon cancer as a part of the primary operation grew out of experiences with reoperations for lymph-node-positive colic cancers.

To what extent enlargement of the primary operation will contribute to a greater number of 5-year conversions remains to be seen. Undoubtedly it is an item of real importance. It is significant that in the last 2 years only five of the 23 second-look procedures performed for lymph-node-

TABLE 6.—Cancer of the ovary: reoperation on 14 patients with positive lymph nodes (41 operations); CANCER FOUND AT SECOND LOOK, 11 patients, 34 operations

Status*	Number of patients	Length of follow-up after first operation (months)
Living and well, last look negative	2	63, 60
Living and well, awaiting another look	1	55
Dead of cancer	6	Range: 22-198 Average: 63.7
Operative deaths	2	9, 6

\*As of June 1, 1963.



TABLE 7.—Cancer of the ovary: reoperation on 14 patients with positive lymph nodes (41 operations); NO CANCER FOUND AT SECOND LOOK, 3 patients, 7 operations

Status*	Number of patients	Length of follow-up after first operation (months)
Living and well, last look, negative	2	124, 47
Living and well, awaiting another look	1†	49

\*As of June 1, 1963.

†Three positive looks 22, 29, and 39 months after first look was negative.

positive cancer had residual cancer. During the first 10 years of this program, approximately 50 percent of lymph-node-positive patients subjected to reoperation had residual cancer.

### SUMMARY

The second-look program is 15 years old. During these years 226 patients with lymph-node-positive cancers of the stomach, colon, or rectum had 312 reoperations (tables 8, 9, 10, 11, 12, and 13). Of the 46 patients with colon cancer whose first reoperation was positive, 4 are cancer-free, a salvage rate of 8.7 percent. Although the achievements in the stomach and rectum groups are less rewarding, the over-all salvage rate for all three groups is 6 percent. The salvage rate and general results have been more encouraging in smaller groups of patients with retroperitoneal sarcomas and ovarian malignancies. Many individuals have lived a pro-

TABLE 8.—Cancer of the stomach: reoperation on 68 patients with lymphatic metastases (93 operations); CANCER FOUND AT SECOND LOOK, 38 patients, 59 operations

Status*	Number of patients	Length of follow-up after first operation (months)
Living and well, last look negative for residual cancer	2	158, 86
Living and well, awaiting another look	1	21
Living with residual cancer	1	10
Dead of cancer	30	Range: 6-61 Average: 18.4
Dead, other than cancer	1	95
Operative deaths	3	30, 23, 23

\* As of June 1, 1963.

longed asymptomatic time before succumbing to their disease. Moreover, valuable information has been gained regarding lymph node spread permitting more effective planning of primary procedures.

TABLE 9.—Cancer of the stomach: reoperation on 68 patients with lymphatic metastases (93 operations); NO CANCER FOUND AT SECOND LOOK, 30 patients, 34 operations

Status*	Number of patients	Length of follow-up after first operation (months)
Living and well	19	Range: 12-145 Average: 86.3
Dead of cancer	7	68, 64, 54, 48, 39, 36, 14
Dead, other than cancer	4	88, 75, 56, 36

\*As of June 1, 1963.

TABLE 10.—Cancer of the colon: reoperation on 101 patients with lymphatic metastases (143 operations); CANCER FOUND AT SECOND LOOK, 46 patients, 85 operations

Status*	Number of patients	Length of follow-up after first operation (months)
Living and well, last look negative for residual cancer	3	177, 172, 141
Living and well, awaiting another look	1	34
Living with residual cancer	2	13, 10
Dead of cancer	32	Range: 8-70 Average: 22.5
Dead, other than cancer	1	133
Operative deaths	7	23, 22, 13, 12, 10, 6, 5

\*As of June 1, 1963.

TABLE 11.—Cancer of the colon: reoperation on 101 patients with lymphatic metastases (143 operations); NO CANCER FOUND AT SECOND LOOK, 55 patients, 58 operations

Status*	Number of patients	Length of follow-up after first operation (months)
Living and well	42	Range: 7-207 Average: 72.2
Dead of cancer	5	62, 54, 51, 41, 28
Dead, other than cancer	7	61, 60, 55, 41, 40, 31, 22
Operative deaths	1	10

\*As of June 1, 1963.

TABLE 12.—Cancer of the rectum: reoperation on 57 patients with lymphatic metastases (76 operations); CANCER FOUND AT SECOND LOOK, 28 patients, 41 operations

Status*	Number of patients	Length of follow-up after first operation (months)
Living and well, last look negative for residual cancer	1	136
Living and well, awaiting another look	1	93
Dead of cancer	25	Range: 10-55 Average: 27. 2
Operative deaths	1	40

\*As of June 1, 1963.

TABLE 13.—Cancer of the rectum: reoperation on 57 patients with lymphatic metastases (76 operations); NO CANCER FOUND AT SECOND LOOK, 29 patients, 35 operations

Status*	Number of patients	Length of follow-up after first operation (months)
Living and well	18	Range: 24-168 Average: 85
Dead of cancer	8	74, 69, 59, 31, 23, 20, 13
Dead, other than cancer	3	60, 58, 55

\*As of June 1, 1963.

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## Summary of General Discussion

The discussion following the papers presented on malignant tumors of the stomach concentrated on two main subjects: 1) the comparability of survival data between countries and between various clinics and 2) the relative merit of various surgical techniques.

### 1. Comparability of survival data derived from cancer registries and various clinics:

(a) The reliability of the diagnosis of malignancy in cases not histologically confirmed seemed of great importance in this site, since the proportion of cases thus confirmed varied considerably in materials from the various registries. Attention was drawn to some studies that had failed to demonstrate any over-diagnosing of cancers of the stomach in such materials.

(b) Attention was also drawn to the fact that in some countries, in a rather large proportion of older patients, the diagnosis was based only on clinical examination of far-advanced cases. It seemed quite conceivable that this might introduce inaccuracies in deciding the origin of tumors first diagnosed after dissemination of tumor tissue in the abdominal cavity had taken place.

(c) It was pointed out that variation between countries in the organization and practice of medical care could influence the comparability of survival data in registry materials, for example, variation in the proportion of cases treated in highly specialized clinics (teaching hospitals).

(d) The comparability of staging was also questioned, particularly in cases not subjected to tumor-directed surgery.

(e) The possibility was mentioned of different prognoses in various histological types of tumors of the stomach. Mention was made of studies undertaken to evaluate the importance of the pathological characteristics of the tumors.

(f) Also discussed was that the comparability of survival data probably would be influenced by variation in the proportion of early detected cases.

(g) The most important factor limiting comparability of survival data from various clinics was found to be the selection of patients referred to and entering specific clinics.

### 2. There was some discussion of the relative merits of various surgical techniques both as regards to survival itself and to "quality of survival" in individual patients.

The discussion also touched on the reported decrease in mortality from cancer of the stomach. It was suggested that the reported decrease in Denmark may be related to increased diagnostic accuracy resulting from more frequent hospitalization of patients with suspected cancer of the stomach. However, the reported decreases in Norway and the United States do not appear to be due to a shift in classification of tumors to other sites.

## Large Intestine and Rectum

End Results in Cancers of the Large Intestine and Rectum. SIDNEY J. CUTLER and WILLIAM I. LOURIE, JR., USA

Cancer of the Large Intestine and Rectum: Comparative Data From Connecticut and Norway, 1953-1958. HENRY EISENBERG, USA, TORBJØRN MORK, Norway, and ROGER R. CONNELLY, USA

Cancer Detection Studies of the Rectum. VICTOR A. GILBERTSEN and OWEN H. WANGENSTEEN, USA

Results of Surgery for Cancer of the Colon and Rectum at the University of Minnesota Medical Center, 1940-1954. OWEN H. WANGENSTEEN and VICTOR A. GILBERTSEN, USA

### GENERAL DISCUSSION

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Presented at the International Symposium on End Results of Cancer Therapy, Sandefjord, Norway, September 16-20, 1963.





## End Results in Cancers of the Large Intestine and Rectum

SIDNEY J. CUTLER *and* WILLIAM I. LOURIE, JR., *National Cancer Institute,<sup>1</sup> Bethesda, Maryland*

THE data pertaining to the three Scandinavian countries (Denmark, Finland, and Norway) and from the State of Connecticut (USA) provide a basis for comparing the total experience in four countries in the management of cancers of the large intestine and rectum. Although completeness of reporting varies to some extent, the tumor registries in these four areas strive to collect information on all cancers diagnosed among their residents. The data for England and Wales and the combined data for the three central registries in the United States (California, Connecticut, and Massachusetts) do not pertain to patients drawn from a defined population. They do, however, represent a very broad experience of a large number of hospitals. For the United States, the Connecticut data provide a check on the representative nature of the combined data (U.S. Central).

The cases reported to the French tumor registry are restricted to patients seen in 22 cancer centers that generally specialize in radiotherapy. Since surgery is the treatment of choice in cancers of the intestinal tract, relatively few patients with cancers of the large intestine and rectum were seen in the hospitals reporting to the French tumor registry. No attempt will therefore be made to interpret the French data, although they are included in the Appendix tables.

Data from all five countries are available on patients diagnosed during the first half of the 1950's. In addition, data on patients diagnosed during 1945-49 are available for Denmark, England and Wales, and the United States. This analysis deals primarily with comparisons based on patients diagnosed during the 1950's, although changes between the two calendar periods are discussed.

<sup>1</sup> National Institutes of Health, Public Health Service, U.S. Department of Health, Education, and Welfare.

## RELIABILITY OF DIAGNOSIS

Every case of cancer of the large intestine and rectum diagnosed by a physician was included to make possible a comparison of the total experience in each country.<sup>2</sup> To evaluate the reliability of the diagnosis, information was requested as to whether the diagnosis was ever confirmed by a microscopic examination of tissue. Data on microscopically confirmed cases are shown separately.

In the United States, 9 of every 10 diagnoses of cancer of the intestinal tract were microscopically confirmed. In contrast, less than 6 of 10 diagnoses were confirmed in Finland. In England and Wales and in Norway the proportion of cases with microscopically confirmed diagnoses was a little less than 7 of 10. In each of the four countries mentioned, the proportion of confirmed cases was about the same for the two major subdivisions—large intestine and rectum. In Denmark, however, 80 percent of cancers of the rectum were microscopically confirmed compared to only 67 percent of cancers of the large intestine (tables 1a and 1b).

The relatively low percentage (67%) of confirmed cancers of the large intestine in Denmark would not be surprising, if a significant proportion

TABLE 1a.—Cancers of the large intestine diagnosed 1950-54\*: survival rates for cases with and without microscopic confirmation of the diagnosis

Sex and country	Number of patients	Microscopically confirmed (%)	Classified as localized (%)	5-Year corrected survival rate (%)		
				All stages		
				All patients	Con- firmed cases	Not con- firmed
Males						
Denmark	1, 531	68	†	26	34	9
England and Wales	2, 085	66	36	30	42	5
Finland	334	55	33	20	31	5
Norway	827	68	41	25	34	2
U.S. Central‡	2, 602	89	38	38	42	7
Connecticut	1, 220	86	41	36	40	8
Females						
Denmark	1, 695	67	†	29	37	10
England and Wales	2, 655	67	36	30	40	8
Finland	535	58	39	21	29	6
Norway	903	63	45	28	39	2
U.S. Central‡	3, 262	90	38	43	45	12
Connecticut	1, 506	87	39	42	46	9

\*Data for England and Wales pertain to cases diagnosed 1952-53; data for Finland and Norway pertain to 1953-56.

†Data on patients with localized cancers of the large intestine were not available for Denmark.

‡Combined data from central registries in the States of California, Connecticut, and Massachusetts.

<sup>2</sup> Cases on which information was obtained solely from death certificates were excluded, since data on survival time are unavailable on these cases. Cases first diagnosed at autopsy were also excluded.

TABLE 1b.—Cancers of the rectum diagnosed 1950-54\*: survival rates for cases with and without microscopic confirmation of the diagnosis

Sex and country	Number of patients	Microscopically confirmed (%)	Classified as localized (%)	5-Year corrected survival rate (%)		
				All stages		
				All patients	Confirmed cases	Not confirmed
Males						
Denmark	1,986	80	45	26	29	12
England and Wales	2,762	69	40	32	42	6
Finland	315	59	44	17	28	0
Norway	569	71	49	22	30	2
U.S. Central†	2,223	92	40	36	38	6
Connecticut	1,028	91	35	37	40	9
Females						
Denmark	1,278	79	44	32	37	9
England and Wales	1,865	71	39	34	43	10
Finland	408	60	49	25	37	5
Norway	416	67	49	25	34	3
U.S. Central†	1,784	92	41	42	44	10
Connecticut	820	90	42	39	41	12

\*Data for England and Wales pertain to cases diagnosed 1952-53; data for Finland and Norway pertain to 1953-56.

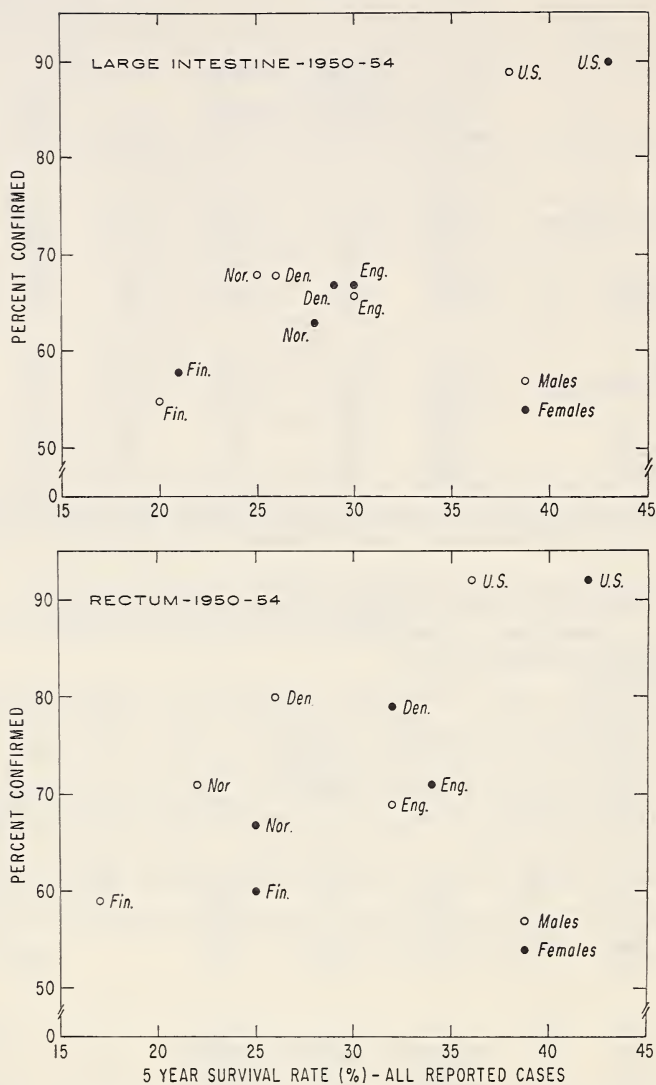
†Combined data from central registries in the States of California, Connecticut, and Massachusetts.

of cases tabulated under "surgery" were in fact limited to a bypass operation. (Problems in the definition of "surgery" are discussed in the section on method of treatment.)

The frequency with which cancer diagnoses are microscopically confirmed is influenced by a variety of factors, such as the availability of hospital facilities for treatment of cancer and the availability of adequately trained surgeons and pathologists. In fact, the percentage of microscopically confirmed diagnoses is sometimes used as a rough index of the "quality" of cancer case management. It is therefore interesting that, for cancers of the large intestine and rectum, there is a positive association between the percentage of microscopically confirmed diagnoses and the 5-year survival rate (text-fig. 1).

## STAGE OF DISEASE

In general, the percentage of rectal cancers classified as localized, *i.e.*, tumor confined to the organ of origin, was a little higher than for cancers of the large intestine. However, the difference was relatively small in spite of the accessibility of the rectum to direct examination. For example, in the United States, 40 percent of cancers of the rectum were classified as localized compared to 38 percent of cancers of the large intestine.



TEXT-FIGURE 1.—Relationship of 5-year survival rate for all reported cases to percent of all cases classified as *confirmed*, by country.



It is generally accepted that there is a direct relationship between early diagnosis and prognosis. A higher percentage of localized cases should be accompanied by a higher survival rate. We find this to be so when we compare two calendar periods for the same country. For example, among male patients with cancers of the rectum the trends were as follows:

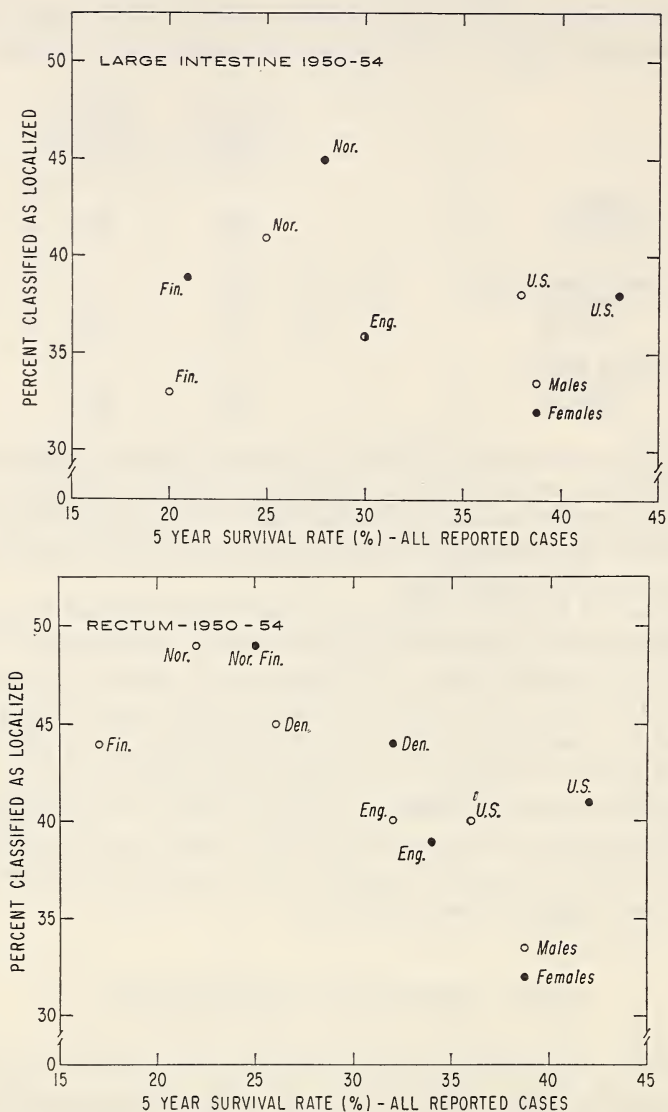
	Classified as localized (%)	5-Year corrected survival rate (%)
Denmark		
1945-49	43	24
1950-54	45	26
England and Wales		
1948-49	35	26
1952-53	40	32
United States		
1945-49	36	27
1950-54	40	36

However, when we compare different countries during the same calendar period (1950-54), we do not find a positive association (text-fig. 2). In fact, there appears to be a negative association for cancers of the rectum, *i.e.*, the higher the percentage of cases classified as localized, the lower the survival rate for the total group.

The absence of a positive association between survival and the percentage of cases classified as localized suggests a lack of uniformity in staging cancers of the intestinal tract. The intent was to evaluate the extent of disease on the basis of all information obtained during the first course of treatment. Exclusion of information obtained from the surgical specimen would tend to overstate the percentage of localized tumors. Even if all registries included information obtained from the surgical specimen in classifying stage, the extensiveness of the resection and the thoroughness with which the operative specimen was examined would materially influence the accuracy of the classification.

## TOTAL SURVIVAL EXPERIENCE

End results of therapy are measured here in terms of the 5-year corrected survival rate, which is the ratio of the observed survival rate to the rate expected in a population similar to the patient group but free of the specific cancer under consideration. The expected rates were based on the general population life tables for each country, taking into account the sex and age characteristics of the patient group. Thus, the corrected survival rate adjusts for variations in the observed survival of cancer patients that may be due to differences in the risk of dying from other



TEXT-FIGURE 2.—Relationship of 5-year survival rate for all reported cases to percent of all cases classified as *localized*, by country.

causes. It is thus possible to compare survival rates pertaining to groups of patients that vary with respect to general mortality risk.

The relationship of survival rates for two countries will depend on the nature of the series being compared. For example, the relationship of the rates for male patients with rectal cancers diagnosed in England and the United States during the 1950's depends on whether cases without microscopic confirmation of the diagnosis are included. The situation is summarized in the following table:

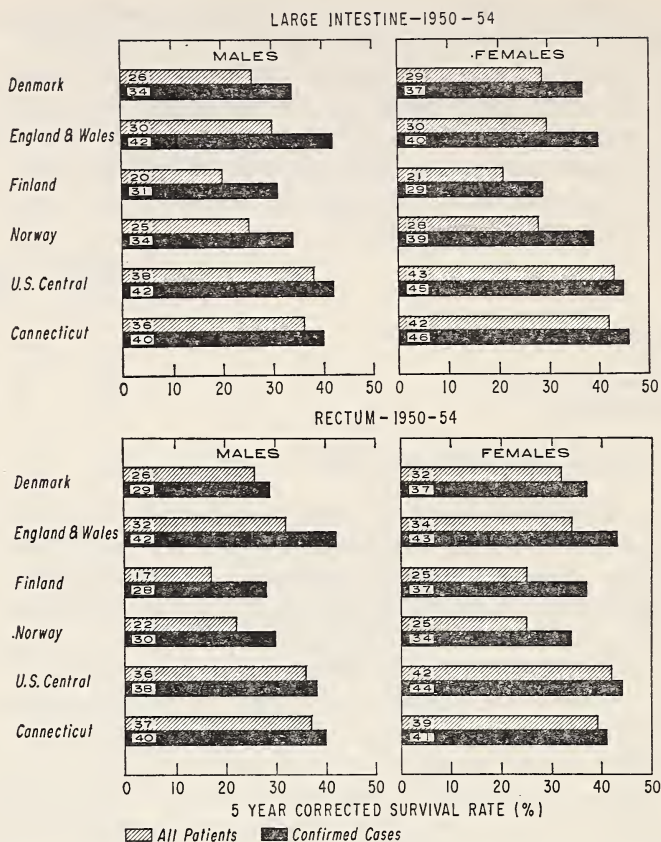
	England and Wales	United States
5-Year corrected survival rate (%) for:		
All patients	32	36
Confirmed cases	42	38
Not confirmed cases	6	6
Percent of cases with microscopic confirmation	69	92

If survival rates for all reported cases are compared, the United States rate is higher; if rates for confirmed cases are compared, the English rate is higher. Survival among unconfirmed cases was equally poor in both countries, but a much higher percentage of diagnoses were not confirmed in England and Wales. As previously indicated, variation in the frequency with which cancer diagnoses are microscopically confirmed depends on a variety of factors. As judged by the low survival rates for unconfirmed cases in all countries (tables 1a and 1b), it is reasonable to assume that a high proportion of such cases are diagnosed in a far-advanced stage. The frequency with which cancer is diagnosed in a late stage is at least in part influenced by the promptness with which patients seek medical attention and the expeditiousness with which physicians obtain a definitive diagnosis.

If the comparison is intended to provide a rough measure of the relative effectiveness of cancer control activities, the survival rates should be based on all diagnosed cases of cancer, whether or not the diagnosis was microscopically confirmed. (The effect of completeness of reporting on the comparison of survival rates is discussed in the paper by Eisenberg and Mork.) On the other hand, if the intent is to compare the results of specific therapeutic procedures, it is best to restrict the series to confirmed cases.

For both large intestine and rectum, survival rates in the United States were higher than in the other four countries, for all reported cases. This was true for both sexes. There was little difference between the rates in Connecticut and the rates for the combined central registries in the United States (text-fig. 3).

The corrected survival rate adjusts for normal mortality risk associated with age, but it does not adjust for other factors associated with age that may influence the survival of cancer patients. For example, surgical inter-



TEXT-FIGURE 3.—Survival rates for all reported cases and for confirmed cases, by country.

vention is used less often in older persons. The tabulations prepared for this Symposium do not provide much detail on the age distribution of patients with cancers of the intestinal tract; only two age groups were used, under 65 and 65 and over. However, this crude classification is sufficient to indicate that the age distributions in the different countries did vary. For example, in Norway 36 percent of male patients with cancer of the rectum were under 65 years of age compared with 45 percent in the United States. (The number of patients under 65 years of age is given in tables 2a and 2b.) It is therefore interesting to determine whether relationships observed for all ages combined would be significantly modified by adjustment for variation in the age distribution of patients. Examination of tables 2a and 2b indicates that this is unlikely. The difference between survival rates in the United States and in the other four countries is about as large for patients under 65, as for patients of all ages combined.



TABLE 2a.—Cancers of the large intestine diagnosed 1950–54\*: survival experience of patients under 65 years of age at diagnosis

Sex and country	5-Year corrected survival rate (%)				
	Number of patients	All patients	Total	Confirmed cases	
				Localized tumors	
				All treat-ments	Treated by surgery
Males					
Denmark	632	30	36	†	†
England and Wales	896	33	42	56	56
Finland	186	25	35	53	66
Norway	326	29	36	55	59
U.S. Central‡	1, 174	41	43	68	71
Connecticut	530	38	41	64	68
Females					
Denmark	779	34	40	†	†
England and Wales	1, 298	33	41	58	59
Finland	258	26	31	53	55
Norway	327	38	44	68	69
U.S. Central‡	1, 622	46	48	77	79
Connecticut	770	45	48	76	78

\*Data for England and Wales pertain to cases diagnosed 1952–53; data for Finland and Norway pertain to 1953–56.

†Data on patients with localized cancers of the large intestine were not available for Denmark.

‡Combined data from central registries in the States of California, Connecticut, and Massachusetts.

TABLE 2b.—Cancers of the rectum diagnosed 1950–54\*: survival experience of patients under 65 years of age at diagnosis

Sex and country	5-Year corrected survival rate (%)				
	Number of patients	All patients	Total	Confirmed cases	
				Localized tumors	
				All treat-ments	Treated by surgery
Males					
Denmark	818	32	34	50	53
England and Wales	1, 210	35	42	58	59
Finland	147	15	22	30	36
Norway	207	26	31	55	62
U.S. Central‡	1, 002	40	41	68	71
Connecticut	503	41	42	68	71
Females					
Denmark	656	37	40	59	69
England and Wales	928	37	43	60	60
Finland	191	31	41	53	64
Norway	160	31	39	60	65
U.S. Central‡	905	45	47	75	78
Connecticut	429	40	42	68	72

\*Data for England and Wales pertain to cases diagnosed 1952–53; data for Finland and Norway pertain to 1953–56.

‡Combined data from central registries in the States of California, Connecticut, and Massachusetts.

## METHOD OF TREATMENT

In this analysis, discussion of method of treatment and associated survival rates is confined to microscopically confirmed cases. Information on all reported cases, confirmed and not confirmed combined, is included in the Appendix tables. The classification of treatment is limited to the first course of therapy.

The agreed-upon definition of "surgery" pertains to procedures in which tumor tissue was removed, but is not restricted to resections in which the primary tumor was removed in its entirety. Due to variations in local coding practices, some registries were not able to adhere to this definition in converting to the "uniform code." The British and Danish registries distinguish between radical and palliative surgery. "Radical surgery" is defined as the removal of the primary tumor and of lymph nodes with possible metastases. "Palliative surgery" includes partial removal of known cancerous growth as well as bypass operations for the relief of symptoms. Thus, the definition of "surgery" in the uniform code is more inclusive than "radical surgery," but excludes bypass operations, which are included under "palliative surgery." Examination of the available data indicates that the British cases tabulated under "surgery" probably include patients treated by "palliative surgery," since the proportion of

TABLE 3a.—Cancers of the large intestine with microscopically confirmed diagnoses; all stages combined, diagnosed 1950-54\*: survival rates by method of treatment†

Sex and country	Number of patients	5-Year corrected survival rate (%)				
		Percent treated by:		Patients treated by:		
		Surgery	Surgery + radiation	All patients	Surgery	Surgery + radiation
Males						
Denmark	1, 035	84	3	34	37	26
England and Wales	1, 368	87	1	42	47	†
Finland	184	35	20	31	55	35
Norway	566	76	1	34	44	†
U.S. Central§	2, 305	82	1	42	50	11
Connecticut	1, 051	82	0	40	48	†
Females						
Denmark	1, 138	84	3	37	41	46
England and Wales	1, 784	85	0	40	46	†
Finland	312	45	18	29	45	41
Norway	571	76	1	39	50	†
U.S. Central§	2, 933	83	1	45	53	11
Connecticut	1, 310	85	1	46	54	†

\* Data for England and Wales pertain to cases diagnosed 1952-53; data for Finland and Norway pertain to 1953-56.

† "All patients" includes patients who received no tumor-directed therapy during the first course of treatment. Data on radiation and chemotherapy are given in the Appendix tables.

‡ Rate not computed. Less than 10 cases in this category.

§ Combined data from central registries in the States of California, Connecticut, and Massachusetts.

TABLE 3b.—Cancers of the rectum with microscopically confirmed diagnoses; all stages combined, diagnosed 1950-54\*: survival rates by method of treatment†

Sex and country	Num- ber of patients	5-Year corrected survival rate (%)				
		Percent treated by:		Patients treated by:		
		Surgery	Surgery + ra- diation	All patients	Surgery	Surgery + ra- diation
Males						
Denmark	1, 579	72	11	29	36	13
England and Wales	1, 897	88	1	42	46	10
Finland	185	51	14	28	43	24
Norway	404	70	2	30	39	§
U.S. Central†	2, 053	74	0	38	48	§
Connecticut	931	79	0	40	48	§
Females						
Denmark	1, 009	72	13	37	45	21
England and Wales	1, 322	89	2	43	47	20
Finland	245	52	16	37	55	36
Norway	280	73	3	34	42	§
U.S. Central†	1, 642	76	1	44	55	7
Connecticut	736	79	1	41	50	§

\*Data for England and Wales pertain to cases diagnosed 1952-53; data for Finland and Norway pertain to 1953-56.

† "All patients" includes patients who received no tumor-directed therapy during the first course of treatment. Data on radiation and chemotherapy are given in the Appendix tables.

‡ Combined data from central registries in the States of California, Connecticut, and Massachusetts.

§ Rate not computed. Less than 10 cases in this category.

cases in this category ("surgery") is unusually high (tables 3a and 3b). This may also be true of the Danish data. Unfortunately, the extent to which "surgery" is overstated in the tabulated data is not known. It is likely that this problem is minimal among cases classified as having localized disease.

The distribution of microscopically confirmed cases by method of treatment and the corresponding survival rates are given in tables 3a and 3b and 4a and 4b. Surgery was the usual method of treatment for cancers of the large intestine and rectum. In Finland, however, a sizable proportion (14-20%) of patients were treated by a combination of surgery and radiation. This was true for cases classified as localized, as well as for cases that had spread beyond the organ of origin. The use of combination therapy was also relatively frequent in Denmark for cancers of the rectum (11-13%). Survival among patients treated by surgery plus radiation was consistently lower than among patients treated by surgery alone. This probably reflects the selection of patients with less favorable prognosis for the combined-treatment method.

Comparison of survival rates for specific subcategories is difficult, because of variation in the definition of stage of disease and method of treatment. In any case, relationships observed in a specific subgroup are generally reflected in the comparison of broader groupings of cases.

TABLE 4a.—Cancers of the large intestine with microscopically confirmed diagnoses; cases classified as localized, diagnosed 1950-54\*†: survival rates by method of treatment‡

Sex and country	Num- ber of patients	Percent treated by:		5-Year corrected survival rate (%)		
		Surgery	Surgery + radi- ation	Patients treated by:		
				All patients	Surgery	Surgery + radi- ation
Males						
England and Wales	637	97	1	57	58	§
Finland	71	58	30	49	63	40
Norway	253	88	1	54	58	§
U.S. Central ¶	931	90	1	66	70	§
Connecticut	472	90	0	62	68	§
Females						
England and Wales	827	98	0	59	59	§
Finland	138	70	22	49	53	52
Norway	269	90	0	60	65	§
U.S. Central ¶	1, 174	95	0	73	76	§
Connecticut	559	96	0	72	75	§

\*NOTE: Data on patients with localized cancers of the large intestine were not available for Denmark.

†Data for England and Wales pertain to cases diagnosed 1952-53; data for Finland and Norway pertain to 1953-56.

‡"All patients" includes patients who received no tumor-directed therapy during the first course of treatment.

Data on radiation and chemotherapy are given in the Appendix tables.

§Rate not computed. Less than 10 cases in this category.

¶Combined data from central registries in the States of California, Connecticut, and Massachusetts.

TABLE 4b.—Cancers of the rectum with microscopically confirmed diagnoses; cases classified as localized, diagnosed 1950-54\*: survival rates by method of treatment†

Sex and country	Num- ber of patients	Percent treated by:		5-Year corrected survival rate (%)		
		Surgery	Surgery + ra- diation	Patients treated by:		
				All patients	Surgery	Surgery + ra- diation
Males						
Denmark	776	80	9	42	47	20
England and Wales	979	95	1	59	60	†
Finland	103	64	17	35	42	30
Norway	212	82	2	45	51	†
U.S. Central §	872	86	0	63	69	†
Connecticut	435	90	0	64	68	†
Females						
Denmark	480	76	13	56	65	32
England and Wales	655	95	1	61	61	†
Finland	148	64	18	51	64	40
Norway	155	79	5	44	49	†
U.S. Central §	699	89	0	70	75	†
Connecticut	328	91	0	65	70	†

\*Data for England and Wales pertain to cases diagnosed 1952-53; data for Finland and Norway pertain to 1953-56.

†"All patients" includes patients who received no tumor-directed therapy during the first course of treatment.

Data on radiation and chemotherapy are given in the Appendix tables.

‡Rate not computed. Less than 10 cases in this category.

§Combined data from central registries in the States of California, Connecticut, and Massachusetts.



For example, among female patients under 65 years of age, with localized cancers of the large intestine treated by surgery, the survival rate was 79 percent in the United States compared to rates of 55 to 69 percent in the other countries (table 2a). This differential is reflected in the rates for all female patients with microscopically confirmed intestinal cancers (all ages, all stages, and all treatments combined)—the survival rate in the United States was 45 percent compared to rates of 29 to 40 percent in the other countries (table 3a). We will therefore limit ourselves to a brief summary of survival rates for all microscopically confirmed cases. Data for various subgroups are given in the tables.

Among male patients, 5-year corrected survival rates were clearly lower in the Scandinavian countries than in England and the United States:

	Males	
	5-Year corrected survival rate (%)	
	Large intestine	Rectum
Denmark	34	29
Finland	31	28
Norway	34	30
England and Wales	42	42
United States	42	38

The same was true among female patients with rectal cancers. The Scandinavian rates were from 34 to 37 percent compared to 43 and 44 percent for England and the United States. The rates for female patients with intestinal cancers fall into a somewhat different grouping:

Intestine—Females	
	Rate (%)
Finland	29
Denmark	37
Norway	39
England and Wales	40
United States	45

The observed differences cannot be explained readily from the available data. For example, the percentages of localized cancers of the rectum treated by surgery was about the same in Denmark, Norway, and the United States (70–74%). The survival rate, however, was considerably higher in the United States (table 3b). The observed difference may have resulted from variation in surgical and other therapeutic procedures. It may, however, be due in part to differences in the criteria used in classifying the stage of disease. On the other hand, differences in the gross and histological characteristics of rectal

cancers may be an important factor. These issues cannot be resolved from the information available on the punched cards at hand. The required information can be obtained only through careful review of individual case histories and of histological specimens.

### CHANGES OVER TIME

Information on patients diagnosed in two calendar periods, the late 1940's and the early 1950's, is available for Denmark, England, and the United States. The observed trends were similar in the three countries—in the later period, diagnoses were microscopically confirmed more frequently, a higher percentage of cases were classified as localized, patients were treated more frequently by surgery (alone), and the survival rates at 5 years increased (tables 5a and 5b).

Although 5-year survival rates increased in each of the three countries, the magnitude of the increase varied, particularly for cancers of the rectum. For example, among male patients with cancers of the rectum, the 5-year corrected survival rate increased by 9 percentage points in the United States—from 27 percent for patients diagnosed in the period 1945–49 to 36 percent for patients diagnosed in the period 1950–54. The corresponding increases in England and in Denmark were 6 and 2 percentage points, respectively (table 5b).

Generally, the magnitude of the increase from the first to the second calendar period was directly proportional to the level of the survival rate in the earlier period, *i.e.*, the higher the survival rate during the earlier period, the larger the increase. This relationship is summarized in the following table:

	5-Year corrected survival rate (%)					
	Males			Females		
	Period I	Period II	Difference	Period I	Period II	Difference
Large intestine						
Denmark	20	26	6	21	29	8
England	21	30	9	23	30	7
U.S. Central	28	38	10	36	43	7
Rectum						
Denmark	24	26	2	26	32	6
England	26	32	6	28	34	6
U.S. Central	27	39	9	33	42	9

This variation in the magnitude of change in survival rates between calendar periods is in part a reflection of variation in the magnitude of changes in the percentage of cases classified as localized and in the percentage of cases treated by surgery (tables 5a and 5b). However,

TABLE 5a.—Cancers of the large intestine: comparison of patients diagnosed in 1945-49 and in 1950-54

Country and years of diagnosis	Number of patients	Microscopically confirmed (%)	Classified as localized (%)	Confirmed cases (%) treated by surgery:		5-Year corrected survival rate (%)		
				All stages	Localized	All patients	Confirmed cases	
							All stages	Localized
Males								
Denmark 1945-49 1950-54	1, 273 1, 531	52 68	* *	81 84	* *	20 26	30 34	* *
England and Wales 1948-49 1952-53	1, 703 2, 085	52 66	28 36	82 87	97 97	21 30	35 42	57 57
U.S. Central† 1945-49 1952-53	1, 901 2, 602	79 89	35 38	73 82	87 90	28 38	34 42	55 66
Females								
Denmark 1945-49 1950-54	1, 385 1, 695	55 67	* *	80 84	* *	21 29	29 37	* *
England and Wales 1948-49 1952-53	1, 926 2, 655	57 67	30 36	82 85	97 98	23 30	36 40	55 59
U.S. Central† 1945-49 1950-54	2, 426 3, 262	81 90	35 38	78 83	89 95	36 43	41 45	67 73

\*Data on patients with localized cancers of the large intestine were not available for Denmark.  
†Combined data from central registries in the States of California, Connecticut, and Massachusetts.

TABLE 5b.—Cancers of the rectum: comparison of patients diagnosed in 1945-49 and in 1950-54

Country and years of diagnosis	Number of patients	Microscopically confirmed (%)	Classified as localized (%)	Confirmed cases (%) treated by surgery:		5-Year corrected survival rate (%)	
				All stages	Localized	All patients	Localized
Males							
Denmark							
1945-49	1,934	71	43	66	76	24	46
1950-54	1,986	80	45	72	80	26	42
England and Wales							
1948-49	2,532	60	35	89	96	26	54
1952-53	2,762	69	40	88	95	32	59
U.S. Central*							
1945-49	1,971	86	36	66	82	27	49
1950-54	2,223	92	40	74	86	36	63
Females							
Denmark							
1945-49	1,262	70	43	67	80	26	50
1950-54	1,278	79	44	72	76	32	56
England and Wales							
1948-49	1,611	59	36	86	95	28	60
1950-54	1,865	71	39	89	95	34	61
U.S. Central*							
1945-49	1,503	86	39	70	84	33	58
1950-54	1,784	92	41	76	89	42	70

\*Combined data from central registries in the States of California, Connecticut, and Massachusetts.



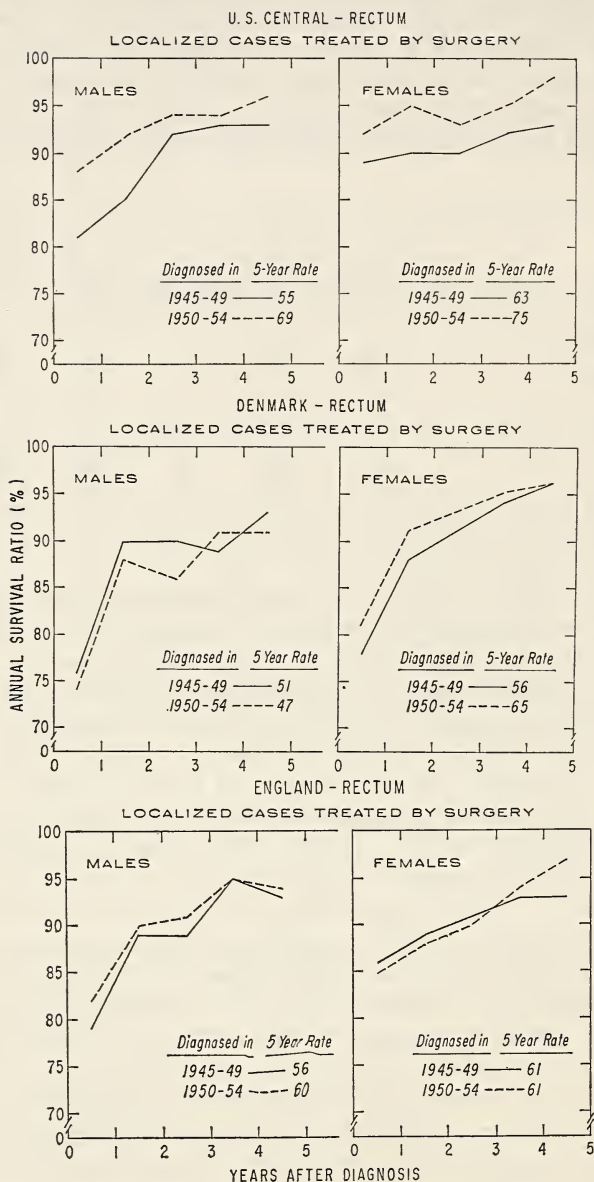
similar variation among the three countries is apparent when survival rates are restricted to surgically treated patients with microscopically confirmed localized tumors. Although the definitions of "localized" and of "surgery" may vary from country to country, it is reasonable to assume that within each country the same definitions were used for patients diagnosed in each of the two calendar periods. The 5-year corrected survival rates for patients with surgically treated, localized cancers were as follows:

	Males			Females		
	Period I	Period II	Difference	Period I	Period II	Difference
Large intestine*						
England	58	58	0	57	59	2
U.S. Central	62	70	8	74	76	2
Rectum						
Denmark	51	47	-4	56	65	9
England	56	60	4	61	61	0
U.S. Central	55	69	14	63	75	12

\*Data for localized cases of intestinal cancer were not available for Denmark.

These figures indicate that in the United States survival rates increased for patients with tumors that originated in both the large intestine and the rectum and for both men and women. There was no consistency to changes in survival rates in Denmark and England. This suggests that a significant change in surgical procedures occurred in the United States and that similar changes did not take place in Denmark and England. The pattern of annual survival rates for each of the first 5 years after diagnosis (and treatment) tends to support this interpretation. To illustrate this point, annual survival ratios (corrected survival rates) for surgically treated, localized cancers of the rectum are shown in text-figure 4. In the United States, survival was consistently higher for patients treated in the later calendar period during each of the first 5 years among both male and female patients. One would expect this type of change if more extensive surgery was used during the later period and if more extensive resection in fact reduces the probability of recurrence. In contrast, the changes in annual survival ratios in Denmark and in England were relatively small, somewhat erratic from one follow-up interval to the next, and inconsistent between male and female patients. This suggests that the observed changes in Denmark and in England may have occurred by chance.

In spite of the observed upward trend, the survival experience of patients with cancers of the large intestine and rectum leaves no room for complacency. For example, the most favorable survival for a total patient group was observed among female patients in the United States—



TEXT-FIGURE 4.—Annual survival ratios: localized cases of cancer of the rectum treated by surgery; United States, Denmark, and England.

a 5-year corrected rate of 42 percent. The complement of this rate ( $100 - 42 = 58$ ) is a measure of excess mortality and indicates that 6 of every 10 patients expected to survive 5 years on the basis of general population experience, in fact, died. Even in the most favorable prognostic group (surgically treated patients with localized disease—U.S.) 3 of every 10 patients expected to survive died within 5 years of diagnosis.

### SUMMARY

Survival rates for patients with cancers of the large intestine and rectum are compared for five countries—Denmark, England, Finland, Norway, and the United States. In general, survival rates were higher in the United States and England than in the three Scandinavian countries.

Information on patients diagnosed in two calendar periods, the late 1940's and the early 1950's, is available for Denmark, England, and the United States. The observed trends were similar in the three countries—in the later period, diagnoses were microscopically confirmed more frequently, a higher percentage of cases were classified as localized, patients were treated more frequently by surgery (alone), and the survival rates at 5 years increased. In spite of the observed upward trend, the survival experience of patients with cancers of the large intestine and rectum leaves no room for complacency.





## Cancer of the Large Intestine and Rectum: Comparative Data From Connecticut and Norway, 1953-1958

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AN international comparative study of cancer survival experience in various countries was presented at the Eighth International Cancer Congress. Cutler and Lourie<sup>5</sup> reported on an analysis of histologically confirmed cases of cancer of the large intestine from five countries. This study revealed that significant differences existed between countries in the 5-year survival rates for patients with malignant neoplasms of the large intestine. Among the findings reported in this study were the following:

- 1) Among male patients, 5-year relative survival rates were very similar in Norway, Denmark, and Finland, with the rate in the United States being significantly higher.
- 2) Among female patients, the rates were similar in Norway, Denmark, and England, with the United States rate again being significantly higher.
- 3) Separate tabulations for the State of Connecticut revealed the same contrasts with the European data.

Such intercountry differences may be due to any of several factors: the definition and classification of diagnostic entities; the histological characteristics of the tumor; the age distribution of the patients; the stage

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<sup>5</sup> Presented at the Eighth International Cancer Congress, Moscow, July, 1962.

and localization of the tumor; methods of treatment or even surgical techniques; data derived from urban and rural areas; or in coding procedures.

Both Connecticut and Norway have comprehensive cancer registration schemes covering total populations, namely, the State of Connecticut and the Country of Norway. It was decided to use the materials from these registries to carry out a more detailed analysis to elucidate possible causes for the observed differences in survival experience. Furthermore, the study was expanded to include all diagnoses (clinical as well as histologically confirmed) of cancer of the entire lower intestinal tract (rectum and large intestine). Analyses by age, stage of disease, and type of treatment were repeated, only in more detail, and analyses by site of tumor origin within the lower intestinal tract and by geographic residency were included.

### REGISTRY BACKGROUNDS

In Norway the registration scheme covers the total population of the country and is based on compulsory reporting of all new cases of malignant neoplasms. According to rules laid down by the Ministry of Social Affairs, reports are required from (a) all hospitals, (b) all institutes of pathology, and (c) all institutes and departments of radiology. In addition, all the official death certificates in which tumors are mentioned are matched against the file of registered cases, and for the cases not found in the registry, queries are sent to the certifying physicians to obtain as detailed information as possible on the case. The registration of cases under this scheme is assumed to be very complete for all parts of the country and all segments of the population.

In Connecticut, the reporting of all cancer cases is on a voluntary basis, as had been originally requested by the medical profession through its State Medical Society 30 years ago. Thirty of the 37 licensed general hospitals in the State, representing almost 94 percent of the acceptable general hospital beds in Connecticut, have been submitting cancer case records to the Central registry. In addition, three hospitals located in adjacent States and also various agencies outside the State have been submitting cancer case records on all patients who were Connecticut residents. Furthermore, the Central registry receives photostatic copies of all death certificates from the Section of Vital Statistics, Connecticut State Department of Health, on which mention of cancer is made. It is believed that there are few if any unreported cancer cases and that the sources of information about cancer patients, upon which the Central tumor registry is built, provide a reasonably complete record of cancer illness among residents of Connecticut. Therefore, presumably all data drawn from the Connecticut Tumor Registry are based on a defined and total population, the State of Connecticut.

## MATERIALS

Not included in the material from either the Norway or Connecticut registries are: patients with carcinomas *in situ* or carcinoid tumors; cases of unknown age; cases coded as intestinal tract, part unspecified; and cases which are subsequent primaries of the lower intestinal tract when the first primary was also of the lower intestinal tract.

Patients having only clinical diagnoses of cancer as well as histologically confirmed diagnoses are included in this study, because it was deemed desirable to investigate the survival experience of *all* patients with lower intestinal tract cancer diagnosed in these two defined populations. Of the total Connecticut material, 77 percent have histologic confirmation of the diagnoses as compared to 68 percent of the total Norwegian material.

The Norwegian material consists of the following: 4,185 cases of carcinoma of the large intestine and rectum reported to the cancer registry of Norway as diagnosed in Norway during the 6-year period 1953-58 (termed analytic cases), 42 cases for which a death certificate was the only source of information (termed d.c. only cases), and 38 cases for which a tumor was unexpectedly discovered at autopsy (termed autopsy only cases), for a total 4,265 cases.

The Connecticut material for the same sites and for the same time period consists of the following: 5,817 analytic cases, 1,941 death certificate only cases, and 99 autopsy only cases for a total of 6,957 cases.

Table 1 shows the percentage distributions for patients included from the two registries by age at diagnosis and basis of diagnosis for each sex.

The diagnosis of carcinoma of the lower intestinal tract is based on death certificate information for 14 percent of the Connecticut material in contrast to only 1 percent of the Norwegian material. This can easily be explained. As previously pointed out, when cancer is mentioned on a Norwegian death certificate and the case is not located in the Central registry, a query is sent to the certifying physician to obtain as detailed information as possible on the case. In many instances enough information is obtained to classify the case as analytic rather than as diagnosed from death certificate information only. However, such queries were not undertaken in Connecticut during the period reported here. In order that the total material from each registry be entirely compatible, it was considered necessary to include the death certificate only cases for each registry in the subsequent analyses whenever possible.

Only a small percentage of each registry's material, about 1 percent, is diagnosed only from autopsy findings. These cases are included for the sake of investigating all cases of cancer of the large intestine and rectum, regardless of the basis of the diagnosis.



TABLE 1.—Percentage distributions by basis of diagnosis and age at diagnosis: males and females with carcinoma of the lower intestinal tract diagnosed in Connecticut and Norway, 1953-1958

Sex and age at diagnosis	Connecticut				Norway			
	Basis of diagnosis				Basis of diagnosis			
	Total, all cases	Analytic cases	Death certificate only	Autopsy only	Total, all cases	Analytic cases	Death certificate only	Autopsy only
Males								
Number of cases	3,451	2,904	491	56	2,134	2,104	12	18
Percent by diagnosis	100	84	14	2	100	99	1	1
Percent by age:								
Total, all ages	100	100	100	100	100	100	100	100
00-49	8	8	5	5	9	9	8	—
50-59	17	18	9	5	15	15	8	6
60-69	33	35	27	18	28	28	17	17
70-79	29	29	33	50	34	33	50	50
80-98	13	10	27	21	15	15	17	28
Average age (years)	(67.3)	(66.4)	(71.7)	(72.7)	(68.2)	(68.1)	(70.8)	(75.0)
Females								
Number of cases	3,506	2,913	550	43	2,131	2,081	30	20
Percent by diagnosis	100	83	16	1	100	98	1	1
Percent by age:								
Total, all ages	100	100	100	100	100	100	100	100
00-49	11	13	2	2	8	8	—	—
50-59	18	20	7	7	14	14	—	10
60-69	27	30	14	21	25	26	13	20
70-79	28	27	34	42	33	33	17	35
80-98	16	11	43	28	19	18	70	35
Average age (years)	(67.2)	(65.4)	(75.9)	(73.6)	(69.1)	(68.8)	(80.7)	(74.5)



From table 1, the number of males and females within each registry series is seen to be approximately equal. This one-to-one ratio appears to be typical when tumors of the large intestine and rectum are considered together (1).

In the Norwegian material, in both males and females we find a slightly higher proportion of older patients: Among males, 49 percent in Norway are 70 years of age or more compared to 42 percent in Connecticut; similarly, among females, 52 percent compared to 44 percent.

## METHODS

Survival rates were computed for each registry's material cross-classified by sex, detailed primary site, stage of disease, type of treatment, age at diagnosis, and geographic residency. The actuarial method of analysis was employed to compute observed, expected, and relative survival rates for each of the first 5 years following diagnosis. Expected survival rates were based on published life tables appropriate for the material being covered in this study. An IBM 1410 computer of the Connecticut State Department of Health performed the necessary calculations on the data from both registries.<sup>6</sup>

The cut-off date for determining length of survival was July 1, 1961. In the Connecticut series, 232 cases (less than 3%) were lost to follow-up before July 1, 1961, and 8 cases in the Norwegian material were considered lost to follow-up. [Subsequent to date of last contact, lost patients are assumed to experience a survival pattern similar to that of patients remaining under follow-up. In a recent article, Bailar has shown this to be an accurate assumption for a series of Connecticut breast cancer patients (2).]

When differences in survival rates for the two registries are examined and termed "significant," this indicates that a test of significance was undertaken and the two rates differed by more than twice the standard error of the difference.

## RESULTS

### Comparison of Total Cases

The relative survival rates at 5 years are significantly different for both sexes at each year following diagnosis, with the Connecticut rates consistently higher than Norway's: for males—Connecticut 0.38, Norway 0.25; for females—Connecticut 0.41, Norway 0.28. When the nonanalytic

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<sup>6</sup> We are indebted to Patricia C. Campbell and Leslie A. Kralits, from the Connecticut Registry, for programming and executing the computations.

cases are included, considering that they have no 5-year survivors, the Connecticut 5-year relative survival rates are reduced while the Norwegian rates remain unchanged. As a result, the differences in the 5-year relative survival rates, though statistically significant, are only half as large: for males—Connecticut 0.32, Norway 0.25; for females—Connecticut 0.34, Norway 0.28.

### Variation by Detailed Primary Site

Information on the site of origin of the tumor within the lower intestinal tract was only partially available for the d.c. only or autopsy only material. Therefore, the analysis by detailed primary site was restricted to the analytic cases.

Table 2 shows the percentage distributions and 5-year survival rates by detailed site. Within each sex the relative frequencies for the various subdivisions of the lower intestinal tract appear to be almost identical for Connecticut and Norway. However, the registry coding procedures for tumors of the rectosigmoid junction are known to be different. Cancers originating in the rectosigmoid junction in the Norwegian material are coded with cancers of the sigmoid colon, whereas in the Connecticut material they are coded with cancers of the rectum.

To investigate the frequency and survival experience of patients with rectosigmoid tumors, a 20 percent random sample of the Connecticut cases coded as primary site rectum (which include rectosigmoid tumors)

TABLE 2.—Survival analysis by detailed primary site: males and females with carcinoma of the lower intestinal tract diagnosed in Connecticut and Norway, 1953–1958, analytic cases only

Sex and detailed primary site	Analytic cases only					
	Connecticut			Norway		
	Num- ber	Percent	5-Year relative survival rate	Num- ber	Percent	5-Year relative survival rate
<b>Males</b>						
Total, all sites*	2,904	100	.38	2,104	100	.25
Ascending colon	443	15	.36	347	16	.29
Transverse colon	287	10	.34	213	10	.19
Descending colon	145	5	.43	63	3	.35
Sigmoid colon	657	23	.44	523†	25	.30
Rectum	1,235†	43	.36	840	40	.23
<b>Females</b>						
Total, all sites*	2,913	100	.41	2,081	100	.28
Ascending colon	564	19	.41	426	20	.29
Transverse colon	338	12	.45	234	11	.36
Descending colon	201	7	.44	96	5	.24
Sigmoid colon	724	25	.44	528†	25	.31
Rectum	928†	32	.39	646	31	.26

\*Total includes cases coded "Large Intestine. NOS."

†Rectosigmoid tumors are coded "Rectum" in Connecticut and "Sigmoid Colon" in Norway.

was selected. The Connecticut Tumor Registry abstracts for these cases were re-examined to ascertain the exact location of the tumor.

- 1) Of the 243 male and 184 female cases re-examined, it was determined that 30 percent of the males and 39 percent of the females had tumors of the rectosigmoid junction.
- 2) The 5-year relative survival rates were lower for the rectosigmoid cases (0.35 for the males, 0.31 for the females) than for those cases which remained classified as rectum (0.38 for the males, 0.44 for females).

Table 3 shows the result of adjusting the analysis of the entire analytic Connecticut series of lower large bowel tumors by use of rates based on the 20 percent sample.

When the adjustment for rectosigmoid tumors is made, it appears that in Connecticut there are relatively more tumors of the sigmoid colon than in Norway. However, there is little, if any, difference in function between the sigmoid colon and the upper rectum. In any individual the area of transition from sigmoid colon to rectum, *i.e.*, the rectosigmoid junction, is both variable and difficult to establish anatomically and physiologically (3). It therefore seems both logical and valid to concentrate on the combined material under study for tumors of the sigmoid colon, rectosigmoid junction, and rectum. This eliminates any concern over the differences which exist between the two registries in coding the detailed primary site.

TABLE 3.—Survival analysis by primary site adjusted according to the results of the 20 percent random sample: males and females with carcinoma of the lower intestinal tract diagnosed in Connecticut\* and Norway, 1953–1958, analytic cases only

Sex and primary site	Analytic cases only					
	Connecticut			Norway		
	Number	Percent	5-Year relative survival rate	Number	Percent	5-Year relative survival rate
Males						
Total, all sites†	2,904	100	.38	2,104	100	.25
Upper large bowel‡	875	30	.37	623	30	.26
Lower large bowel§	1,892	65	.39	1,363	65	.26
Sigmoid colon	(1,033)	(36)	(.41)	523	25	.30
Rectum	(859)	(30)	(.38)	840	40	.23
Females						
Total, all sites†	2,913	100	.41	2,081	100	.28
Upper large bowel‡	1,103	38	.43	756	36	.31
Lower large bowel§	1,652	57	.41	1,174	56	.28
Sigmoid colon	(1,082)	(37)	(.39)	528	25	.31
Rectum	(570)	(20)	(.44)	646	31	.26

\*Note: Connecticut figures in parentheses are adjusted on the basis of a 20 percent sample of rectum cases to include cases with tumors of the rectosigmoid junction with cases coded sigmoid colon.

†Total includes cases coded "Large Intestine, NOS."

‡Ascending, Transverse, and Descending colon cases.

§Sigmoid colon, rectosigmoid colon, and rectum cases.



The percentage distributions shown in table 3 for lower large bowel tumors are almost identical in the two registries: among males, 65 percent in each registry; among females, 57 percent in Connecticut and 56 percent in Norway. The survival rates for tumors of the lower large bowel and upper large bowel within each registry-sex subgroup are approximately equal.

While the survival rates vary from site to site, there are no instances (table 2 or 3) in which the 5-year survival rate for a subsite is significantly different from the over-all survival rate of its registry-sex subgroup. The analysis by detailed primary site fails to account for the large differences in survival demonstrated between the two registries. In the subsequent analyses by other variables, tabulations are shown only for all detailed sites combined. In any such analysis, distributions and survival rates for the detailed primary sites were found not to affect the conclusions drawn from the analyses of all sites combined.

#### Age at Diagnosis

Table 4 shows the age-specific survival rates for all cases combined, including death certificate and autopsy only cases. The survival patterns by age are quite similar within each registry-sex subgroup: Survival rates for patients under 60 years of age are above the average of the subgroup; patients in their sixties have approximately average survival; patients 70 years of age or over have below average survival. Since relative survival rates are being compared, the excess normal mortality for the older age groups has been taken into account. Therefore, it seems that the

TABLE 4.—Survival analysis by age at diagnosis; males and females with carcinoma of the lower intestinal tract diagnosed in Connecticut and Norway, 1953–1958

Sex and age at diagnosis	Connecticut			Norway		
	Num- ber	Percent	5-Year relative survival rate	Num- ber	Percent	5-Year relative survival rate
<b>Males</b>						
Total, all ages	3,451	100	.32	2,134	100	.25
00–49	267	8	.33	185	9	.31
50–59	577	17	.37	313	15	.31
60–69	1,153	33	.35	593	28	.27
70–79	1,016	29	.27	719	34	.20
80–98	438	13	.22	324	15	.12
<b>Females</b>						
Total, all ages	3,506	100	.34	2,131	100	.28
00–49	380	11	.39	176	8	.42
50–59	615	18	.44	303	14	.33
60–69	954	27	.37	543	25	.28
70–79	985	28	.32	697	33	.23
80–98	572	16	.16	412	19	.16



younger the patient the more favorable the prognosis, even after correcting for normal mortality.

Among male patients, the survival rates for Connecticut cases are consistently higher than for the Norwegian cases within each age group. Among female patients, the youngest and oldest patients in each series have similar survival rates. Connecticut females between 50 and 79 years of age, however, do considerably better than Norwegians of the same age.

Age-adjusting<sup>7</sup> the over-all survival rates for each registry-sex subgroup does not result in reduced differences when comparisons are made between the two registries among males and females. That is, considering the variable "age" by itself, one cannot account for the large differences between the registries in survival.

### Type of Treatment

The material is divided into four treatment groups according to the patient's first course of medical care.

- (a) Radical surgery—resection of that portion of the lower intestinal tract containing the primary site of the tumor (typically abdominal-perineal resection of the rectum and anterior resection of the colon). This treatment category includes cases treated by radical surgery plus radiation or chemotherapy.
- (b) Other definitive surgery—simple extirpation or removal of a part of the intestine containing cancer; includes fulguration, electrodesiccation, extirpation biopsy, and surgery, extent unknown.
- (c) Bypass surgery—surgery not considered tumor-directed therapy since the lesion is merely bypassed, not removed.
- (d) Other and no treatment—cancer treatment other than surgery (typically, radiation); no tumor-directed therapy in the first course of medical care (including exploratory laparotomy). This category primarily consists of "no treatment" cases since very little treatment other than surgery was used.

Table 5 presents the survival experience by type of treatment and age for all cases. There are no statistically significant differences between the two registries in the survival rates for the various treatment categories. For example, among males the 5-year relative survival rates for Connecticut and Norwegian cases treated by radical surgery are 0.46 and 0.42, respectively, and among females 0.51 and 0.48.

The percentage of cases receiving other definitive surgery is higher in Connecticut than in Norway, although in both registries this treatment category contains few cases. The survival rates for this treatment category are similar to those for radical surgery in Norway, and are even higher than for radical surgery in Connecticut. There are substantial differences in the survival rates between the two registries: among males 5-year rates of 0.62 in Connecticut and 0.43 in Norway; among females

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<sup>7</sup> The direct method of standardization was used. To obtain age-standardized rates, the age-specific survival rates for each registry-sex subgroup were applied to the standard age distribution formed by combining all the cases under study.

TABLE 5.—Survival analysis by type of treatment and age at diagnosis: males and females with carcinoma of the lower intestinal tract diagnosed in Connecticut and Norway, 1953-1958

Treatment and age	Males						Females					
	Connecticut			Norway			Connecticut			Norway		
	Num- ber	Percent	5-Year relative survival rate	Num- ber	Percent	5-Year relative survival rate	Num- ber	Percent	5-Year relative survival rate	Num- ber	Percent	5-Year relative survival rate
Total, treated and untreated												
All ages	3,451	100	.32	2,134	100	.25	3,506	100	.34	2,131	100	.28
00-59	844	24	.37	498	23	.31	995	28	.42	479	22	.36
60-69	1,153	33	.35	593	28	.27	954	27	.37	543	25	.28
70-98	1,454	42	.25	1,043	49	.18	1,557	44	.26	1,109	52	.20
Radical surgery												
All ages	2,053	100	.46	1,135	100	.42	2,083	100	.51	1,016	100	.48
00-59	596	29	.46	322	28	.45	745	36	.50	331	33	.50
60-69	765	37	.47	373	33	.42	650	31	.50	323	32	.44
70-98	692	34	.47	440	39	.38	688	33	.53	362	36	.50
Other definitive surgery												
All ages	168	100	.62	30	100	.43	172	100	.56	50	100	.47
00-59	56	33	.63	6	20	.52	53	31	.65	13	26	.58
60-69	56	33	.67	6	20	.38	50	29	.68	8	16	.33
70-98	56	33	.52	18	60	.35	69	40	.32	29	58	.55
Bypass surgery												
All ages	251	100	.00	348	100	.01	263	100	.01	316	100	.02
00-59	54	22	.00	83	24	.02	58	22	.02	57	18	.02
60-69	80	32	.01	94	27	.01	78	30	.01	90	28	.01
70-98	117	47	.00	171	49	.00	127	48	.01	169	53	.03
Other and no treatment												
All ages	979	100	.02	621	100	.02	988	100	.01	749	100	.03
00-59	138	14	.03	87	14	.04	139	14	.03	78	10	.04
60-69	252	26	.01	120	19	.00	176	18	.00	122	16	.04
70-98	589	60	.02	414	67	.02	673	68	.01	549	73	.02

0.56 and 0.47. However, these differences are not significant, being based on such small numbers of patients.

Patients receiving bypass surgery have as dismal a survival prospect as those receiving other and no treatment. There are very few 5-year survivors in either registry for patients not receiving definitive treatment. The 5-year relative rates range from 0.00 and 0.03 for the bypass surgery and other and no treatment categories.

Table 5 indicates that the decrease in survival rates with age, as shown in table 4, is primarily a result of the more favorable treatment distribution for the younger patients. Within each treatment category, the survival rates decrease with increasing age in only a few minor instances. In fact, the age-adjusted survival rates for each treatment category are in most every case identical to the unadjusted rates shown in table 5.

### Urban and Rural Regions

People living in the rural areas of the State of Connecticut are essentially as accessible to hospital facilities as are people living in the largest towns of the State. This is certainly not true in Norway. Therefore, analyses were carried out on the Norwegian material by use of the same residence grouping (based on local administrative areas) used by the Norwegian Central Bureau of Statistics for census purposes.

- (a) *Urban*—cities and towns varying in population from approximately 450,000 to approximately 2,000.
- (b) *Densely populated*—local administrative areas in which 50 percent or more of the total population is living in a geographical clustering of houses, each group of houses having at least 200 residents. Many of these areas have a considerably larger population than some of the areas administratively designated as urban.
- (c) *Rural*—administrative areas with lower population density than in the previous categories.

The percentage distributions of cases by region, age, and detailed primary site are shown in table 6. There are no striking differences between the three regions in regard to age at diagnosis or detailed primary site, although males from urban and densely populated regions are slightly younger than males from rural regions.

The 5-year relative survival rates for all patients by urban, densely populated, and rural regions are, respectively: among males, 0.29, 0.26, and 0.20; among females, 0.30, 0.26, and 0.26. In comparisons with Connecticut, the data for the densely populated region are grouped with the urban region under the assumption that the medical facilities in urban and densely populated regions of Norway are comparable to those for the entire state of Connecticut. In all subsequent discussions the combined urban and densely populated regions are termed "urban."





## Stage of Disease

The classification scheme used for staging the disease is based on all information available at the time of first discharge from the hospital and is somewhat different from the scheme adopted by the International Ad Hoc Group on End Results.

- (a) *Localized*—cancer strictly confined to the site of origin; lesions primary in the bowel wall with extension into the pericolic tissues but not involving other organs.
- (b) *Regional*—metastases to local or regional lymph nodes.
- (c) *Distant*—cancer passing the bounds of the site of origin and involving neighboring organs, tissues, lymphatics, or blood vessels; metastases to distant organs or lymph nodes.
- (d) *Unknown*—cancer with unknown extent of disease.

Even though the definitions for staging agreed upon by the two registries are strictly adhered to, problems and inconsistencies in the coding of stage of disease can and probably do exist, possibly resulting in differences between the two registries concerning stage of disease. There are obvious difficulties in distinguishing between localized tumors and those with regional spread, especially among those patients not surgically treated. For this reason the combined stages, localized and regional, are often used in analysis of the data.

Table 7 presents the percentage distributions by stage and treatment for the entire Connecticut series and by urban and rural regions for Norway. Within each registry series, the stage distributions for males and females are almost identical. The stage distributions are also very similar for the urban and rural regions of Norway. Between the two registries, however, there are substantial differences. In Norway the proportion of cases staged localized is larger than in Connecticut and the proportion staged regional is correspondingly smaller, with the proportion of distant-unknown cases being approximately the same in each series (though not directly shown in table 7, this relationship exists within each treatment category also).

The treatment distributions for males and females in Connecticut are almost identical. For all stages combined, 59 percent in both sexes received radical surgery. About 81 percent of males and females staged localized or regional received radical surgery compared to 25 percent or less among cases staged distant-unknown.

In Norway the treatment distributions differ for males and females and also by region. Males have a more favorable treatment distribution, at least among the urban residents. Also, a higher percentage of radical surgery is performed in the urban regions than in the rural regions for both sexes.

For all stages combined, the treatment distributions for urban Norwegian residents are similar to those for Connecticut, at least more so than those for rural Norwegians. Unlike Connecticut, however, cases

TABLE 7.—Percentage distributions by region, stage of disease, and type of treatment: males and females with carcinoma of the lower intestinal tract diagnosed in Connecticut and Norway, 1953-1958

Sex and type of treatment	Connecticut			Norway-urban*			Norway-rural		
	Stage of disease			Stage of disease			Stage of disease		
	Total all stages	Local-ized	Regional	Distant and unknown	Total all stages	Local-ized	Regional	Distant and unknown	Total all stages
<b>Males</b>									
Number of cases	3,451	1,263	867	1,321	1,203	585	223	395	931
Percent by stage	100	37	25	38	100	49	19	33	100
Percent by treatment:									
Total, treated and untreated	100	100	100	100	100	100	100	100	100
Radical surgery	59	81	81	25	59	73	86	21	46
Other definitive surgery	5	8	3	3	1	2	0	1	2
Bypass surgery	7	3	7	12	15	8	9	29	18
Other and untreated	28	8	10	60	25	17	4	49	34
<b>Females</b>									
Number of cases	3,506	1,225	970	1,311	1,245	582	207	456	886
Percent by stage	100	35	28	37	100	47	17	37	100
Percent by treatment:									
Total, treated and untreated	100	100	100	100	100	100	100	100	100
Radical surgery	59	81	82	22	51	64	87	18	43
Other definitive surgery	5	9	3	3	2	4	1	0	3
Bypass surgery	8	3	6	13	15	9	8	25	15
Other and untreated	28	7	8	63	32	23	3	57	40

\*Includes "densely populated" regions.

staged localized in Norway have surprisingly lower proportions of patients receiving radical surgery than do cases staged regional in Norway.

Table 8 shows the survival experience by region and stage for all cases, treated and untreated, and also for radical surgery cases only. Comparing the survival rates for the two regions in Norway, large differences are observed between urban and rural males not only for all cases combined but even for patients receiving radical surgery. Such regional differences are smaller or nonexistent, however, among the Norwegian females.

Considering stage of disease, there are strikingly large differences between registries in the survival rates for cases staged localized. Large differences are observed even for those patients with localized disease treated by radical surgery. Possible explanations of these differences are covered in the Discussion.

## DISCUSSION

The data presented are derived from two central tumor registries, the Norwegian registry and the Connecticut registry, both of which are collecting data from defined population groups. In this material, all diagnoses, whether histologically confirmed or clinical diagnoses only, are included. The percentage of histologically confirmed cases in Connecticut is higher than in Norway, 77 percent as compared to 68 percent. However, 98 percent of patients receiving radical surgery have histological confirmation of the tumor in both registries. The higher percentage of cases histologically confirmed in Connecticut is attributable to the fact that more radical surgery is performed in Connecticut than in Norway, 59 percent as compared to 50 percent.

The survival experience for both males and females in the Connecticut series is substantially higher than for the Norwegian cases, even with the inclusion of the nonanalytic cases. The cause of these differences has been investigated with regard to primary site of the tumor within the large intestine and rectum, age, stage, treatment, and geographic residence.

The analysis by detailed primary site reveals some variations in relative frequencies and survival rates between the two registries. However, these variations, even after adjusting for coding differences, have no effect on the large over-all differences in survival rates demonstrated between the two registries.

Even though the Norwegian series is comprised of slightly older cases, and older patients have a less favorable prognosis, age at diagnosis in itself does not account for the large differences in survival that are demonstrated.

Considering the findings with regard to type of treatment, in Connecticut there are a larger percentage of cases treated by definitive surgery and a smaller percentage of cases receiving only bypass surgery or other



TABLE 8.—Survival analysis by region, type of treatment, and stage of disease: males and females with carcinoma of the lower intestinal tract diagnosed in Connecticut and Norway, 1953-1958

	Connecticut			Norway-urban*			Norway-rural		
	Number	Percent	5-Year relative survival rate	Number	Percent	5-Year relative survival rate	Number	Percent	5-Year relative survival rate
<b>Males</b>									
Total, treated and untreated	3,451	100	.32	1,203	100	.28	931	100	.20
All stages	1,263	37	.63	585	49	.46	423	45	.34
Localized	867	25	.26	223	19	.24	151	16	.19
Regional	2,130	62	.48	808	67	.40	574	62	.30
Localized and regional	1,321	38	.05	395	33	.05	357	38	.03
Distant and unknown									
Radical surgery									
All stages	2,053	100	.46	704	100	.45	431	100	.37
Localized	1,020	50	.69	429	61	.59	247	57	.49
Regional	701	34	.30	192	27	.28	132	31	.22
Localized and regional	1,721	84	.53	621	88	.49	379	88	.40
Distant and unknown	332	16	.12	83	12	.15	52	12	.15
<b>Females</b>									
Total, treated and untreated	3,506	100	.34	1,245	100	.29	886	100	.26
All stages	1,225	35	.68	582	47	.45	400	45	.43
Localized	970	28	.31	207	17	.35	153	17	.22
Regional	2,195	63	.51	789	63	.42	553	62	.37
Localized and regional	1,311	37	.06	456	37	.05	333	38	.08
Distant and unknown									
Radical surgery									
All stages	2,083	100	.51	634	100	.48	382	100	.48
Localized	997	48	.73	372	59	.59	210	55	.64
Regional	800	38	.37	181	29	.38	124	32	.25
Localized and regional	1,797	86	.56	553	87	.52	334	87	.50
Distant and unknown	286	14	.19	81	13	.19	48	13	.31

\*Includes "densely populated" regions.



and no treatment than in Norway. Connecticut cases treated by definitive surgery have slightly higher survival rates than in Norway, but these rates are not significantly different. In fact, no statistically significant differences exist between the two registries for any treatment category. When the registry survival rates for each treatment category are applied to a standard treatment distribution (the treatment distribution for all cases combined), the large differences demonstrated for the survival rates between registries are substantially reduced: the treatment-adjusted rates are: among males, 0.29 in Connecticut, 0.26 in Norway; among females 0.31 and 0.30. That is, the large differences between the two series of cases in favor of Connecticut appear to be due to the more frequent use of definitive surgery in Connecticut than in Norway.

In an endeavor to explain the existing differences between Connecticut and Norway in treatment distributions, an analysis by stage and geographic residence was made. Connecticut can be considered an urban area, especially for the purposes of analyzing data on cancer treatment and survival, since it has been estimated that less than 5 percent of its population lives on farms, and all places within the State are in easy reach of a medical facility. Norway, on the other hand, has a definite rural component of low density populations. In this study, such areas are defined as "administrative areas," in which more than half of the working population is occupied in farming, forestry, and fisheries, and lives in other sparsely populated areas. The analysis of the material in this manner by urban and rural regions revealed essentially identical distributions by stage of disease, but strikingly different distributions by type of treatment. Among urban Norwegian residents a higher percentage of radical surgery is performed than in rural areas. As a result, the treatment distributions for urban Norwegian residents are more nearly comparable to those of the Connecticut series. This result is reflected in the survival rates, the urban Norwegians experiencing more favorable survival. In fact, there are no statistically significant differences between the survival rates in Connecticut patients and urban Norwegian patients, though the Connecticut survival rates are consistently higher: among males 0.32 for Connecticut, 0.28 for Norway urban; for females 0.34 and 0.29. However, in contrast to this, Connecticut compared to rural Norway shows among Connecticut males a 5-year survival rate of 0.32 to 0.20 for Norway, among Connecticut females 0.34 to 0.26 in rural Norwegian females.

In considering stage of disease, where no significant differences exist between the registries within any treatment category for all stages combined, cases staged localized show substantial differences even for cases treated by radical surgery. However, it seems more logical to assume that these differences are at least partly due to dissimilarities between the two registries in the staging of cases rather than to accept the fact of better survival for cases staged localized in Connecticut. This becomes

particularly apparent when one realizes that for all cases, treated and untreated, 96 percent of those staged localized in Connecticut are histologically confirmed, while the percentage in Norway is only 75 percent. The unexpected differences among localized cases, all treatment categories combined, might be due to the fact that, in Norway, cases without surgery and those for whom there is no knowledge of metastases eventually are classified by the reporting doctors as localized cases, while in Connecticut such cases would probably be classified as stage unknown. However, in the radical surgery treatment category, similar differences among localized cases exist. Since 98 percent of the radical surgery cases are histologically confirmed in both registries, the above explanation would probably not hold.

## CONCLUSIONS

The major findings of this study are:

- 1) The over-all survival experience for patients with cancer of the lower intestinal tract is better in Connecticut than in Norway.
- 2) Those patients in Connecticut and Norway receiving definitive surgery have similar and relatively good survival rates, while those not treated definitively have similar and quite poor survival rates.
- 3) The observation that more definitive surgery is performed in the Connecticut registry material than in the Norwegian accounts for a large part of the over-all difference between the registries in their survival rates.
- 4) The large rural component in Norway, where less definitive surgery is performed than in the urban and densely populated regions, largely accounts for the fact that more definitive surgery is performed in Connecticut than in Norway.

Several questions remain unanswered:

- 1) What is the explanation for the unexpected observations concerning stage of disease? For example, though the survival rates for patients treated by radical surgery are similar in the two registries there are large differences in favor of Connecticut among those patients with tumors staged localized.
- 2) What factors account for the differences observed between the urban and rural regions in Norway? For example, though the survival rates for females in either region are similar, the urban males do appreciably better than the rural males even when the comparison is restricted to males treated with radical surgery.
- 3) How are the findings of this study regarding survival rates related to the statistics on the incidence and mortality for cancer of the intestinal tract in Connecticut and Norway?

Studies of the data obtained from international cancer registries, as undertaken by the Ad Hoc Group on International Cooperation in Evaluation of End Results, though often not leading to definitive conclusions, offer many interesting clues for further investigation. This

study was conducted as a result of the findings reported by the Ad Hoc Group, and other special studies similar in depth to this one may be necessary for better international comparison of end results. It may also be worthwhile to investigate further the findings of this study, perhaps through a joint investigation carried out by registry personnel and surgeons well acquainted with the techniques used for study of cancer of the large intestine and rectum in Connecticut and Norway.

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## Cancer Detection Studies of the Rectum<sup>1, 2</sup>

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THE Cancer Detection Center program of annual physical examinations of asymptomatic patients was established in 1948 at the University of Minnesota and continues as a research activity of the Department of Surgery. The program comprises a study concerned with several aspects of early diagnosis of malignant diseases, and, in addition, serves a useful function in investigative and educational capacities. Each patient is examined annually. Currently, active participants in the program number about 5,000. Reports of the results of the individual examinations are sent to the private physician designated by the patient.

The group of annual examinees is comprised of patients not less than 45 years of age, who are free from signs or symptoms suggestive of malignant or other serious disease on enrollment in the program, who agree to return each year for examination, and who consult their private physicians for recommended therapy or indicated additional investigative procedures.

While examinations performed at the Cancer Detection Center endeavor to evaluate all potential areas of malignancy, particular attention has been afforded to those areas and to those malignancies with the greater frequencies of occurrence. The scheme of examination includes "screening" tests, utilized to minimize failures to identify cancers of the more common sites; such procedures have also permitted an estimation of the efficacy of employment of the tests themselves.

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<sup>2</sup> The University of Minnesota Cancer Detection Center in its early years derived partial support from the Minnesota Division of the American Cancer Society. It operates with the approval and endorsement of the Minnesota State Medical Association and its Cancer Council.

In evaluation of the upper gastrointestinal tract, for example, gastric analyses are performed routinely; patients found to have achlorhydria or hypochlorhydria by this method are selected for X-ray examinations of the upper gastrointestinal tract (1). Further distally in the alimentary canal, proctosigmoidoscopic examinations—most useful in direct visualization of the rectum, rectosigmoid, and distal sigmoid—are performed as part of each annual examination. Other routine procedures include chest X-ray, guaiac stool examination, hemoglobin, leukocyte count, urinalysis, and Papanicolaou cervical smear examination.

During the 15-year period, March 1948 through August 1963, 11,963 patients have participated in the Cancer Detection Center program. These patients have undergone a total of 51,876 examinations, including 39,913 re-examinations performed subsequent to initial visits.

Recently substantial interest has been manifest in problems concerned with earlier diagnosis of colon and rectal cancers and its association with improved prognosis for patients with these lesions. Cancer of the rectum is probably the most readily detectable of all internal cancers (2). Proctosigmoidoscopy allows direct visualization of 20 to 25 cm of the distal bowel, currently the area of involvement of approximately 65 percent of all intestinal cancers, and is impressive because of the ease and facility of its performance when employed routinely by those familiar with the procedure. Since carcinoma of the large intestine, in the United States, presently accounts for more deaths in both sexes from malignant diseases than does cancer primary in any other single organ, this area would appear to merit the attention of those concerned with malignant disease and its early diagnosis.

Routine proctosigmoidoscopy has been part of each of the nearly 52,000 annual examinations performed in this Center since 1948. Abnormalities detected, including polyps, adenomas, malignant lesions, and the like, are reported to private physicians, together with recommendations for removal. Initial proctosigmoidoscopic examinations, performed on these 11,963 patients, resulted in detection of 19 adenocarcinomas, subsequently confirmed microscopically. Since most of these patients had not undergone such an examination in the preceding year, or even during the preceding several years, this incidence, of course, is not presented as an annual rate of development, and, in fact, likely was comprised of lesions which initially developed during any of several preceding years.

Following the initial examination, however, subsequent (or recheck) examination would appear likely to detect such lesions at a rate parallel to those for other similar groups of persons in our country. Thus, an estimation of the number of carcinomas anticipated to develop in the area subject to proctosigmoidoscopic examination during the 39,913 "recheck" patient-years experience in such a group of white persons, with a median age of 55 years, might be made with some degree of accuracy by those familiar with biostatistical methods.

Only 9 such adenocarcinomas, however, were actually detected in these nearly 40,000 recheck annual proctosigmoidoscopic examinations. Two of the 11 originally recorded lesions were not confirmed as malignancies after careful review of the available microscopic sections by our pathologists and must be considered, at most, to represent adenomatous polyps with an area of atypical epithelium. In addition, meticulous follow-up study failed to disclose a single additional adenocarcinoma primary in this area of bowel in any of these 12,000 Cancer Detection Center patients during their period of active participation in the program. Only 2 carcinomas are known to have developed after participation was discontinued; each of these was diagnosed 7 or 8 years after the last examination of these patients in our Center.

Of some interest was the rather sharp localization of each of the 9 lesions detected on recheck examination. Inferentially, we can conclude that none had spread to remote or adjacent organs or to lymph nodes; none had evidence of spread external to the bowel or even through the full thickness of the bowel wall. In 4 carcinomas, malignant changes were entirely confined to the epithelial layer of the bowel. In 4, submucosal invasion had occurred, in each instance sharply localized. In the last, circumscribed invasion of a few malignant glands was found in the muscular layer; in this single instance, the lesion had been observed by the proctologist in this Center 3 years prior to ultimate excision by the private physician.

Seven of the 9 cancers were considered by the several private surgeons responsible for therapy to be sufficiently limited as to require only local excisions, without resection of a segment of bowel. One patient underwent an abdominoperineal resection for a lesion that, on microscopic examination, involved only the mucosa. The single operative death occurred in a patient who underwent a segmental resection for a sigmoid cancer, which microscopically appeared as a small area of adenocarcinoma in a "polyp" with a limited focus of submucosal invasion. All 8 survivors of surgery are presently living and well without signs of recurrent or residual cancer, one 14 years following diagnosis, and 5 of the 8 have been followed for 5 years or more.

## SUMMARY

The Cancer Detection Center program of routine proctosigmoidoscopic examinations, included in the annual physical examinations, appears to have permitted the earlier detection of cancers of the rectum and distal colon. This area may be directly visualized on routine proctosigmoidoscopy and currently is the site of origin of about 10 percent of all fatal cancers in this country. None of the 9 adenocarcinomas found in 40,000 re-examinations represented more than a "localized" lesion. In 4 patients involvement was confined to the mucosa, 4 had submucosal involvement,



and 2 patients subjected to conventional radical operation showed no evidence of lymph node involvement or penetration of the bowel wall on microscopic examination of tissue. Of these 9 patients, only 1 died after surgery; the rest are living and well—one 14 years following simple excision; 6 followed 3 years or more remain well, and 5 of these have been followed 5 years or more.

The data presented are offered as suggestive evidence, rather than statistical proof, that routine proctosigmoidoscopic examinations and the subsequent removal of any suspicious lesions detected may have had a direct causative relationship on the low incidence of adenocarcinomas of this particular bowel area than might otherwise have reasonably been anticipated in a group of patients of this size.

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## **Results of Surgery for Cancer of the Colon and Rectum at the University of Minnesota Medical Center, 1940-1954<sup>1</sup>**

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### **I. CLINICAL ASSESSMENT**

CANCER of the large bowel, including colon and rectum, takes more lives in the United States today than cancer in any other organ, mainly because it involves both sexes about equally. Cancer of the lung and the stomach are primarily cancers of the male. Other frequent cancers, such as those of the prostate, uterine cervix, and the breast, are, in fact, sex determined.

#### **Importance of Early Diagnosis**

Nowhere in the surgical management of malignancy is the worth of early diagnosis more apparent than when cancer of the rectum is dealt with. Figures for our Cancer Detection Center show that the over-all 5-year survival rate following surgical treatment for cancers of the rectum, rectosigmoid, and distal sigmoid in patients who had their cancers diagnosed by recheck annual proctosigmoidoscopic examinations (after initial examinations) in the Center approached 90 percent, and was 100 percent if the single operative death is excluded—a figure which far exceeds our accomplishment in symptomatic patients who come to our hospital outpatient clinic with cancer of the rectum.

Unfortunately, the colon—except for the more distal portion—does not permit endoscopic examination. Instruments now under construction by

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the American Cystoscope Company may ultimately permit visualization as far as the splenic flexure. In the main, however, we depend on roentgen examination for the diagnosis of colic cancer. Because of the difficulty of securing complete evacuation of the bowel, despite a number of enemas, most roentgenologists, at least ours, fully concede they cannot compete with the Scandinavian roentgenographers who report (1955) that with employment of double-contrast media of air and barium, and with careful preliminary preparation of the colon with enemas, they can recognize quite routinely colic polyps or lesions less than 0.5 cm in diameter (1). Such, certainly, is not the experience of most American roentgenographers, many of whom are seeking new techniques with new media for examining the mucosa of the colon [Margulis and others, 1961 (2)].

One of us had the privilege 35 years ago (1928) of attending the First International Cancer Conference held in London. The counsellors of King George V read a message, which has come to be known as the King's Reply (3), in which he stated:

I note with interest that your object is research, both into the cure and causes of cancer. No doubt, in the last resort the discovery of the cause is the only certain and absolute means of cure. But I am glad that you have not ignored the practical side of the problem. Remembering the thousands of sufferers from cancer, I feel that if your discussions lead to advance in diagnosis, treatment, or even palliation of the disease, this Conference will have justified itself and earned the gratitude of mankind.

Many of us then were inclined to believe that the King and his counsellors had underestimated the power of research. However, it appears now that King George V was probably the best cancer prophet of the century, thus far. In 1897, on the occasion of the 50th Anniversary of the American Medical Association, W. W. Keen (4), an acknowledged leader in surgery, expressed the wish he could live another 50 years, for 1947 would surely see the end of the threat of cancer. In this light, King George V has proved a far more realistic prophet.

It may be a long time until the Gordian knot of cancer is unraveled. It may come through more intimate acquaintance with problems of carcinogenesis, as all of us would like to believe it will, thus dealing with the problem at its source. It may come through the development of more specific chemotherapeutic agents, which would prove a great boon to many patients with well-advanced cancer who now are doomed to die. However, it needs to be emphasized that early recognition has no competitor in augmenting the results of energetic surgical treatment. In other words, investigators, as well as clinicians, need to lend increased emphasis and to focus more sharply upon techniques of earlier cancer detection. For the breast, the experience at our Cancer Detection Center indicates that annual physical examination by experienced and interested doctors counts significantly. Ninety percent of patients whose breast cancers were detected in the Center have continued well more than 5 years later. It has been

suggested by some that for breast cancer, too, objective radiologic or other techniques will come about to improve the score of the annual physical examination, although this appears, at best, remote, since the age-adjusted 5-year survival rates are nearly 100 percent.

For the rectum, rectosigmoid, and the lower reaches of the sigmoid—an area accounting for more than 50 percent of all bowel cancers—an annual proctosigmoidoscopic examination will suffice. We still must await, however, techniques adequate in most hands to insure early recognition of the more proximal colic lesions. The same can be said, of course, for the stomach, the lung, and a number of other viscera.

### The Operation for Colic Cancer

The importance of incorporating the removal of lymph nodes as a part of the surgeons' primary operation was learned partially from dealing with cancer of the breast. In reporting the experience of the Billroth Clinic in Vienna, Winiwarter (5) in 1879 stated that among 143 women treated surgically for cancer of the breast, 8 survived 3 to 6 years, a circumstance which lent considerable encouragement to extension of surgical endeavors in dealing with cancer in other areas. Today we find that at least this modest 5 percent of patients will survive without any treatment whatsoever—perhaps an indication of the lateness of diagnosis in those earlier years. Gradually, the concept of removal of lymph nodes, together with excision of the primary lesion, became fairly standard practice, too, for cancer of the colon and rectum. Despite early advocacy of removal of the axillary lymph nodes in the operation for cancer of the breast by the Billroth group of surgeons (1879), Samuel W. Gross (6) of Philadelphia (1880), and Mitchell Banks (7) of Liverpool (1882), Küster (8) of Berlin (1883), many modern-day surgeons still appear to find justification for debating whether the operation of cancer of the breast should include removal of the lymph nodes in the primary operation.

No one contests this thesis in operations for cancer of the colon and rectum. The main question is how far one should go in execution of the operation. Experienced surgeons concede that the operation considered as radical half a century ago by Ernest Miles (9), having a simultaneous focus on increased length of bowel removal as well as on excision of the entire regional lymphatic drainage area, is a minimal requirement for the ultimate success of an adequate operative procedure for other than localized cancers of the rectum.

In cancer of the colon, excision of the juxta-lying regional lymphatic drainage area and lymph nodes in the mesentery became fairly early an integral part of the operation. Moreover, in the early history of excisions for this cancer, primary excision and anastomosis were carried out regularly. However, the formidable mortality persuaded Thomas Bryant



(10) of London (1882), Bloch (11) of Copenhagen (1892), Paul (12) of Liverpool (1895), and Mikulicz (13) of Breslau (1892), to abandon primary excision, substituting in its place what came to be known as the exteriorization operation for obstruction, which Schede (14) of Hamburg had unintentionally performed in 1879. In this procedure, obviously, adequate excision of the lymphatic drainage area was relegated to a position of secondary importance. From the 1890's until the latter part of the third decade of the present century, surgeons quite universally performed the staged operation for most colon cancers because of the high mortality attending primary excision and anastomosis. However, with adoption of the closed anastomosis and the recognition of the role of large bowel obstruction, surgeons found it possible to perform primary resection with relatively low mortality. Primary excision permits more adequate excision of the cancer and its lymphatic drainage area than does the exteriorization operation of Bryant-Bloch-Paul and Mikulicz.

Many surgeons today have added antibiotic preparation of the bowel prior to operation and have abandoned closed anastomosis. In this clinic, however, preliminary preparation of the bowel with cleansing enemas and a precisely executed closed anastomosis continue to be basic to the operation of choice for all colon cancers.

In 1946 we began to perform near or total colectomies for all cancers of the colon distal to the hepatic flexure in standard-risk patients, anastomosing either the ascending colon a few centimeters distal to the ileocecal valve or the very terminal ileum to the rectum (15). Persistent diarrhea infrequently attends this procedure (16). Only when 20 to 30 cm or more of terminal ileum as well as the right half of the colon are sacrificed, as is necessary occasionally in cancers of the cecum with considerable lymph node involvement in the ileocecal angle of the mesentery, does protracted diarrhea sometimes follow. The accompanying examples afford some suggestion concerning the extent of bowel removal in various locations. In standard-risk patients, near or total colectomy can be carried out with approximately the same risk as attends segmental colectomy. Over a

TABLE 1.—Operative mortality, 1940–1954

	Rectum			Colon		
	Num- ber of cases	Operative deaths		Num- ber of cases	Operative deaths	
		Num- ber	Percent		Num- ber	Percent
Regular resections	463	24	5	393	21	5
Enlarged resections*	47	12	26	80	22	27
Colostomies	105	18	17	41	12	29

\*Includes partial hepatectomies, pelvic eviscerations, excisions of adjacent organs, etc.



TABLE 2.—Rectum and colon, 1940–1954

	Rectum (%)	Colon (%)
Operability rate	98	98
Resection rate	82	87
"Crude" 5-year survival rates:		
Over-all	27. 5	32
All cases excised	35	40
Excised for cure	44	52. 5

2-year interval from 1941 to 1943 (17), during which 60 consecutive resections were made of the colon, including the rectosigmoid area, 46 of these resections were for malignancy. One death occurred in these 60 resections (1.6% hospital mortality or 2.1% for the patients with cancer). This figure has not been equaled in this clinic even among our surgeons who have toyed with preoperative antibiotic preparation of the bowel. The mortality for colon resection in standard-risk patients, whether segmental resection or total or near total colectomy was done, was 5 percent. The over-all mortality for all operations for cancer of the colon is given in table 1. The operability, resection rate, and 5-year survival rate are given in table 2.

In an earlier paper (1963), Gilbertsen reported (24) a 10 percent improvement in the 5-year survival of patients with cancer of the right half of the colon for the period 1951–54 as contrasted with the years 1940–50. Similarly for cancers of the left half of the colon, there was an 11 percent improvement over the same period. For multiple sites of origin of the colic cancers, the improvement in a small number of patients for the same period was 220 percent. It would appear, therefore, that the enlarged operation which has become usual practice in standard-risk patients has noticeable dividends in patient survival. In the rectum, on the contrary, over the same years in this clinic, the improvement in survival was only 1 percent. However, as will be outlined, it is not easy to enlarge upon the standard conventional abdominoperineal operation.

### The Rectum

Whether early detection of rectal cancer by annual proctosigmoidoscopic examination in cancer detection centers will ultimately reduce the need for so aggressive an operation as abdominoperineal excision of the rectum, only time will tell. In any event, of 9 patients in whom the diagnosis of adenocarcinoma was made by examinations subsequent to initial examinations in our Cancer Detection Center, 8 remain well. One patient subjected to an anterior resection by his surgeon died of postoperative complications. None of the other 8, 7 of whom were treated by wide, local excision through an operating proctoscope, and 1 who underwent an abdominoperineal excision for a circumscribed lesion, have thus far man-

ifested any evidence of residual cancer. Five have now passed the 5-year mark.

For the more conventional patient with symptomatic clinical cancer of the rectum, lying near the anus, the abdominoperineal operation must be done. For lesions higher than 10 cm above the anus, the results of anterior resection are about as good as those of the more radical abdominoperineal excision of the rectum. It is to be lamented that a cancer so readily susceptible to early diagnosis as rectal cancer should often reach the stage where it has extended beyond the confines of the rectum when the patient comes for treatment.

Surgeons have learned that the conventional abdominoperineal operation for cancer of the rectum is inadequate for many large rectal cancers. Despite the magnitude of the abdominoperineal operation, it is still insufficient for invasive rectal cancer. One need only consider the anatomical boundaries of a rectal cancer deep in the pelvis to appreciate how impossible it is to get several centimeters beyond the lesion on every border. If a rectal cancer in the male has extended through the anterior rectal wall, even though one removes the seminal vesicles and shaves off a thick sliver of the prostate, the abdominoperineal operation often has been inadequate. If the cancer extends laterally, the surgeon can only extend his dissection to the lateral pelvic walls. The number of recurrent rectal cancers in the perineum testifies to the difficulty of ablating a rectal cancer that has penetrated the posterior rectal wall. An earlier operation, undertaken before the cancer has gone through the rectal wall, is the only procedure which can consistently deal effectively with a rectal cancer deep in the pelvis. Apart from more adequate circumferential dissection of the rectum and its cancer in the depths of the pelvis, we have been concerned especially with the problem of the lymph nodes. To remove adequately the lymph-node-bearing area adjacent to the vessels in the true pelvis, the surgeon often wishes he had better exposure. Excision of the synchondrosis of the symphysis, a technique I began to employ in 1954 (18, 19), improves the exposure considerably. A retractor of the Tuffier variety enhances the exposure and makes it easier to do an adequate operation. Placement of a Parham band through the two femoral foramina insures a firm and sturdy closure. During 1954-55, five such operations were done. There is definitely greater disability, initially. However, a stable pelvic girdle is the rule. The gain of a more adequate operation justifies occasional employment of this maneuver to gain better exposure in large, invasive, rectal cancers and in adipose patients.

Our clinical experience with rectal cancer from 1940-54 is indicated in tables 3 through 7. Despite the potential possibility for early diagnosis of rectal cancer, the over-all achievement suggests very definitely that positive and substantial improvement in the accomplishment can come only through recognition of earlier, less invasive lesions.

TABLE 3.—Cancer of the colon

A. ALL RESECTIONS FOR CURE, 1940-1954					
	Number of cases	5-Year survivors		Operative deaths	
		Number	Percent	Number	Percent
+ Nodes*	174	61	35	26	15
— Nodes	190	130	68	10	5
All	364	191	53	36	10

B. REGULAR CURATIVE RESECTIONS					
+ Nodes	106	44	42	7	7
— Nodes†	190	130	68	10	5
All	296	174	59	17	6

\*Node cases in this group include hepatectomies, pelvic eviscerations, and multiple organ excisions.

†Nodes same as in A.

TABLE 4.—Colon cancer, University Hospitals, 1940-1954

	Number of patients	5-Year survivors		Age adjustment for 5-year rate	
		Number	Percent	Factor	Adjusted rate (%)
Localized, excised for cure	190	130	68	78.2	87.5
All cases, excised for cure	364	191	52.5	79.6	68
All cases excised	484	192	40	82.2	48
All cases	594	192	32	79.4	41

TABLE 5.—Cancer of the rectum

A. ALL RESECTIONS FOR CURE, 1940-1954					
	Number of cases	5-Year survivors		Operative deaths	
		Number	Percent	Number	Percent
+ Nodes*	186	46	25	21	11
— Nodes	219	131	60	10	5
All	405	177	44	31	8

B. REGULAR CURATIVE RESECTIONS					
+ Nodes	140	37	26	9	6
— Nodes†	219	131	60	10	5
All	359	168	47	19	5

\*Node cases in this group include hepatectomies, pelvic eviscerations, and multiple organ excisions.

†Nodes same as in A.

TABLE 6.—Rectal cancers, University Hospitals, 1940-54

	Number of patients	5-Year survivors		Age adjustment for 5-year rate	
		Number	Percent	Factor	Adjusted rate (%)
Localized, excised for cure	219	131	60	77. 6	77
All cases, excised for cure	405	177	44	79. 3	55
All cases excised	522	184	35	77. 6	44
All cases	669	184	27. 5	78. 6	35

TABLE 7.—Bowel cancer—1,338 patients, 1940-1954

	Number of patients	5-Year survivors	
		Number	Percent
I. Resections			
A. For cure			
Regular	655	342	55.3
Enlarged	100	20	27.4
Other	43	15	42.9
All	798	377	51.9
B. For palliation			
Regular	175	1	0.6
Enlarged	27	0	0.0
Other	22	2	13.3
All	224	3	1.5
C. Indeterminate	23	6	28.6
D. Total resected	1,045	386	40.6
II. Not resected			
A. Explored			
Colostomy	146	0	0
Bypass	9	0	0
Enterostomy or cecostomy	10	0	0
Laparotomy only	19	0	0
All	184	0	0
B. Inoperable	26	0	0
C. Total not resected	210	0	0
III. Other			
A. Refused treatment	20	0	0
B. Moribund on admission	30	0	0
C. Diagnosis only	33	17	51.5
D. Total "other"	83	17	20. 5

## II. BIOSTATISTICAL ASSESSMENT

Fortunately, we are able to report results on all patients seen during 1940-54; no patient in our group was lost to follow-up (20, 21). Circumstances also permitted microscopic confirmation of virtually all the lesions of the patients included in our group, so that the percentage of "unconfirmed" cases has been considered as negligible. Although shorter



periods of postoperative follow-up may well be valuable in biostatistical evaluation, for simplicity we have limited presentation of our results to 5-year survival rates. Since, heretofore, age-adjustment factors have only infrequently been used in current surgical reports, we have included both the "crude" and the age-adjusted 5-year rates. In calculation of age-adjustment factors, the Berkson-Cutler method was utilized (22, 23). Data are presented in tables 1 and 2 for patients with cancers of the colon and rectum. All patients whether admitted to the hospital and whether considered for surgical therapy have been included. A few, seen only for diagnosis and who went elsewhere for treatment, are excluded; this group is largely comprised of patients with lesions detected at the Cancer Detection Center, and the survival rate of this small group is actually greater than our over-all rates.

Analysis of our follow-up data, we are pleased to note, indicates that for all patients with adenocarcinoma of the rectum (all stages, confirmed and not confirmed) seen at this hospital, 1940-54, the "crude" over-all 5-year survival rate was 27.5 percent, and the 5-year age-adjusted rate was 35 percent. The 35 percent over-all survival rate compares favorably with others for groups of substantial size, previously and presently reported.

Of interest is that in nearly every instance over-all survival rates parallel the calculated percentages of the over-all series subjected to surgical-excision procedures. Of the University of Minnesota series, 70 percent of the patients underwent excisions. Associated with increasing proportions of the over-all series of cases subjected to surgical excisions was an increase in over-all percentage of prolonged survivors.

A genuine lack of uniformity is known to exist even in definition of the several anatomic areas; this appears to be especially true regarding the rectum. In the series from the University of Minnesota Hospitals, we have followed the anatomical nomenclature which defines the rectum as that portion of the large bowel below the third sacral vertebra, including rectum proper and rectosigmoid or approximately a segment extending 16 cm proximal to the anus. The rectosigmoid comprises the short segment of the bowel between the sigmoid proximally and the rectum proper, an area 10 to 16 cm from the anus, embracing a short segment usually not exceeding 6 cm in length. Whether this segment should be classified with the rectum or the colon is probably a matter of opinion, but we have included the rectosigmoid area with the rectum proper.

For the 522 of 669 patients with rectal cancers seen at the University of Minnesota Hospitals from 1940-54 who had their lesions excised, the 5-year age-adjusted survival rate was 44 percent. Follow-up studies of the 219 "confirmed-localized-treated surgically" rectal cancer patients seen at the University of Minnesota Hospitals (1940-54) reveal an age-adjusted 5-year survival rate of 77 percent.

It appears evident that when cases are classified as "localized," validity in formulation of most conclusions regarding comparability of survival rates is necessarily predicated on the assumption of comparably meticulous examinations for evidences of lymph node involvement in excised specimens. In the 1940-54 Minnesota series, during the first several years microscopic examination of lymph nodes was not routinely done; only when gross examination of the specimens by the pathologist indicated a possibility of lymph node involvement was such examination performed. Currently, however, a diligent, routine search is made for lymph nodes, and all that are identified are sectioned for microscopic study. When only nodes which appear grossly involved are examined microscopically, a falsely high number of cases are likely to be considered "localized," and survival rates for such groups might well be anticipated to be substantially lower than would otherwise be true.

From 1940-54, 594 patients with adenocarcinomas of the colon were seen at the University of Minnesota Hospitals, including "all stages, all cases, confirmed and not confirmed." Only the small group seen for diagnosis but treated elsewhere was excluded. The age-adjusted 5-year survival rate of these patients was 41 percent, a figure similar to that for "U.S. Hospital," 1945-54. Observations regarding relationships of over-all survival rates to percentages of patients subjected to surgical excisions also appear to pertain for survival rates of patients with colon cancers. Of 594 patients with colon cancers, 484 (81.5%) underwent surgical excisions, for an age-adjusted 5-year survival rate of 48 percent, a rate similar to that for 1945-54 for "U.S. Hospital," "U.S. Central," Connecticut, France, Norway, and for the limited number of cases from Finland.

In evaluation of the results of surgical therapy it would also appear to be of merit to consider the percentages of excisions undertaken for palliation, those instances in which, although the primary tumor was excised, residual malignancy was definitely known to exist at the conclusion of the operative procedure. Our series of patients who had excisions of bowel cancers includes 21 percent which were performed for palliation. As information available from the current surgical literature indicates that many surgeons perform far fewer palliative excisions, survival figures were separately computed for those who underwent curative excisions. The age-adjusted 5-year rate of survival was 68 percent for the 364 patients who underwent excisions for cure of colic cancers. Our most favorable survival rate was that for the 190 patients subjected to curative surgical excisions for "localized" colon cancers; the age-adjusted 5-year rate of survival was 87 percent, which appears to be a substantial, albeit limited, achievement of survival.

Concerning those patients for whom excisions of bowel lesions are undertaken for cure, the performance of a more completely adequate operative

procedure has its greatest pertinence. It appears likely that no occult factors need be postulated in explanation of the relatively favorable overall rates of survival for patients with bowel cancers seen at the University of Minnesota Hospitals: The majority of these patients who were seen from 1940-54 underwent excisions performed for cure, and most patients with other than localized lesions underwent relatively comprehensive excision procedures (24). Of all patients with rectal or colic cancers, 1940-54, 61 percent underwent surgical excisions for cure; the age-adjusted 5-year survival rates for these was 68 percent for those with colon cancers and 55 percent for patients with cancers of the rectum. Although a number of patients who underwent surgical excisions of "localized" lesions likely have achieved prolonged survival without the necessity of the larger procedures, it is nonetheless noteworthy that the 87.5 percent age-adjusted 5-year survival rate for the 190 patients treated surgically for "localized" colon cancers probably reflects, at least in part, employment of more adequate operative procedures. The 77 percent 5-year rate for the 219 patients who underwent excisions of "localized" rectal cancers also compares favorably with other reported rates.

Obviously once bowel malignancies have spread to the more remote organs, such as lung or liver, cases of "cure" or even of prolonged survival are sufficiently rare to justify individual case reporting. It is equally obvious that the seemingly much less advanced cancers which have penetrated the bowel wall but also have spread to local or regional lymphatics require, for any substantial curative achievement, adequate removal of the areas of spread, including the appropriate lymphatics. Unfortunately, for those patients with cancers which have spread beyond the bowel wall to lymph nodes, even when the more comprehensive surgical procedures have been employed and age-adjustment factors are utilized in analysis of survival rates, survival, with few exceptions, is modest. Furthermore, our follow-up studies of 10 to 15 years' duration for patients treated surgically for cure of lymph node positive cancers primary in the rectal ampulla indicate that fully half of those alive 5 years postoperatively subsequently died with recurrent cancer (24, 26).

The potential accomplishment of more adequate, more extensive surgery, moreover, is not likely to equal the potentiality for improvement in overall survival possible by earlier treatment of a greater proportion of lesions yet localized to the tissue of origin. The experience of the Cancer Detection Center with proctosigmoidoscopy and cancers of that area of bowel appears to suggest evidence that death from cancers primary in this bowel area—presently accounting for about 10 percent of all cancer deaths in the United States—probably can now be considered potentially preventable for patients who undergo annual proctosigmoidoscopic examinations, removal of such benign adenomas as might be detected, and prompt and adequate surgical therapy for malignant lesions which might occur.



## SUMMARY

The accomplishment of surgery in both colic and rectal cancer is definitely better than in gastric cancer. Only, however, when these lesions come to be recognized in early and incipient stages can the results of surgical treatment be improved significantly.

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## Summary of General Discussion

The discussion was first directed at whether a surgical advance might explain the survival increases in the United States. In response, it was stated that the striking surgical improvement in technique had been associated with the greater facility with which the colon could be treated—with no parallel advance for the rectum. The data, however, indicated relatively greater improvement for survival after rectal surgery. Therefore, the idea was advanced that there may have been a change in the criteria used for staging rectal cancers.

Demonstration was made of how the changed classification of a specific subgroup could improve the apparent survival rate for the localized as well as the regional cases, while leaving unchanged the survival rate of the combined localized and regional cases. It was later suggested that the same type of reasoning was pertinent to classification of cases on the borderline of malignancy.

An extended and vigorous discussion focused on the various problems for the pathologist in committing himself to a statement that a particular tumor was or was not malignant at a particular time. It was emphasized that, in contrast to a quantitative reading of a laboratory test, the histological decision is rather an interpretation of various data and is affected by the pathologist's philosophy as well as his assessment of how the resulting statement will be used by his clinical colleagues. The more experienced pathologist is less likely to respond to pleas for greater specificity from the clinician and the statistician than is the junior member of the department. It was recognized that there may be variation in the degree to which borderline cases of malignancy are omitted, and, correspondingly, some benign conditions are "overdiagnosed" as cancer. In this regard, attention was directed to the ratio between data pertaining to Connecticut and to Finland. These two registries were consistently at the upper and lower ends of distributions on colon and rectal cancer mortality, morbidity, and survival rates.

Suggestion was made that a distribution according to hospital size might reveal factors associated with the use of radical treatment.

The study by Mork and Eisenberg was indicated as an example of what could be done in the next phase of development of the program of the Ad Hoc Group. It was also pertinent to a problem cited by Dr. Evang in opening the Symposium. Not only is there something unique in the cancer case distribution in rural Norway, but also the question may be how to get better health services in rural Norway.

## Leukemia

Survival Rates for Leukemia in Various Countries. KNUD LOCKWOOD, BENT STANCKE, and JOHANNES CLEMMESSEN, Denmark

Factors Influencing Survival Time in Patients with Acute Leukemia. JEAN BERNARD, M. BOIRON, A. MANUS, J. P. LEVY, and J. LELLOUCH, France

### GENERAL DISCUSSION

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Presented at the International Symposium on End Results of Cancer Therapy,  
Sandefjord, Norway, September 16-20, 1963.





## **Survival Rates for Leukemia in Various Countries**

KNUD LOCKWOOD, *D.M.Sc.*, BENT  
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A comparison of survival rates for leukemia has been made on the basis of figures from those countries participating in the survey for which the data were comparable.

### **MATERIAL AND METHODS**

The survey includes data from the United States, which is a combination of material from the centralized registries in California, Connecticut, and Massachusetts and a number of teaching hospitals in other parts of the country, and the Norwegian Cancer Registry, the Finnish Cancer Registry, the Danish Cancer Registry, and data from France pertaining to patients seen in 22 cancer centers that generally specialize in radiotherapy.

Differences in definitions of leukemias and clinical tradition on which the data are based may influence to an unknown extent the results of statistical studies. The material collected was too limited for breakdown into age groups; the data from France did not even permit a division of sex. Furthermore, because of high mortality during the first period of treatment, particularly for children, it was preferred to exclude the age group 0-9 years from the study, and consequently rates are given only for the ages between 10 and 98 years, as one group. Thus results must be considered with some reservation.

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<sup>1</sup> The authors are grateful to Miss Marie Lindhardt, D.M.h.c., B.P.Sc., for statistical advice.

Chronic leukemias have been divided into myeloid and lymphatic types. Since acute leukemias are often difficult to differentiate, it was considered best to omit consideration of the different types of such leukemias. Furthermore, the diagnosis of leukemia as acute is made after the patient has been observed for some time, so that a selection of patients with poor prognoses unintentionally takes place.

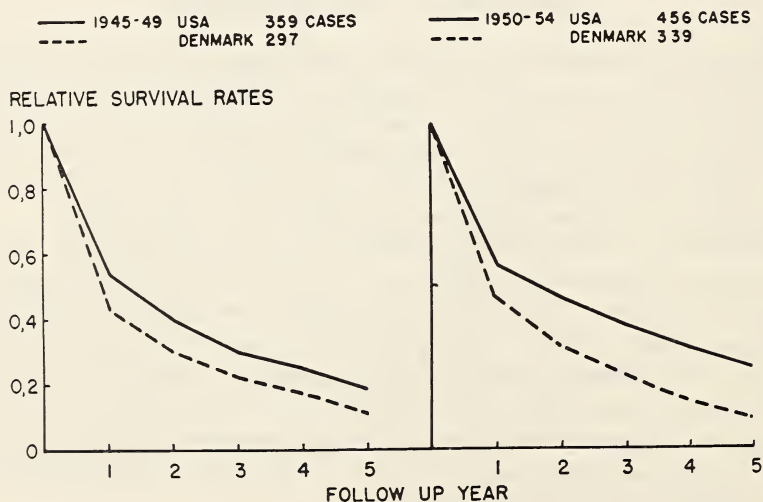
## CHRONIC LEUKEMIA

A comparison was made of the available data from the United States, Denmark, and France.

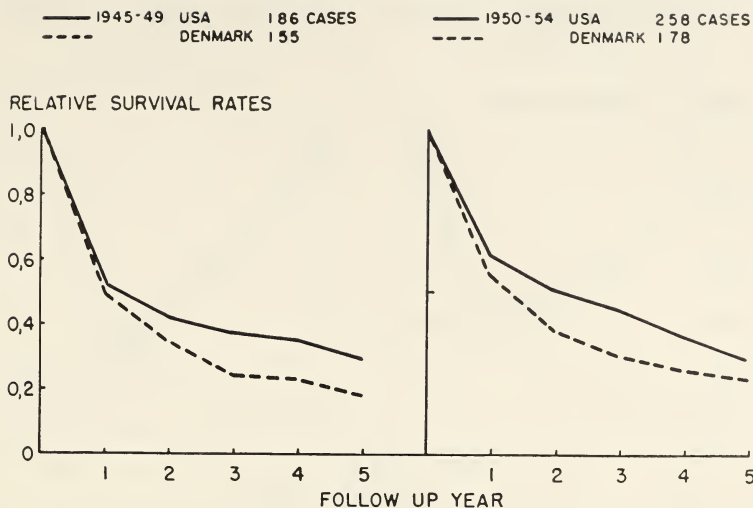
### Chronic Lymphatic Leukemia

It appears from the curves for relative survival rates for the first 5 years that the total rates for treated and untreated cases together are slightly less favorable for the Danish than for the American material during the first year. Since the slope is approximately the same after this period, it may be assumed that the essential difference occurs during the first year and determines the later course. This applies to both sexes.

For comparison of treated cases, those patients treated with irradiation, chemotherapy, and hormones were included. For the years in question a further classification of the limited Danish material was not possible. It may be worth noting that in both the United States and Denmark only half the cases were treated.

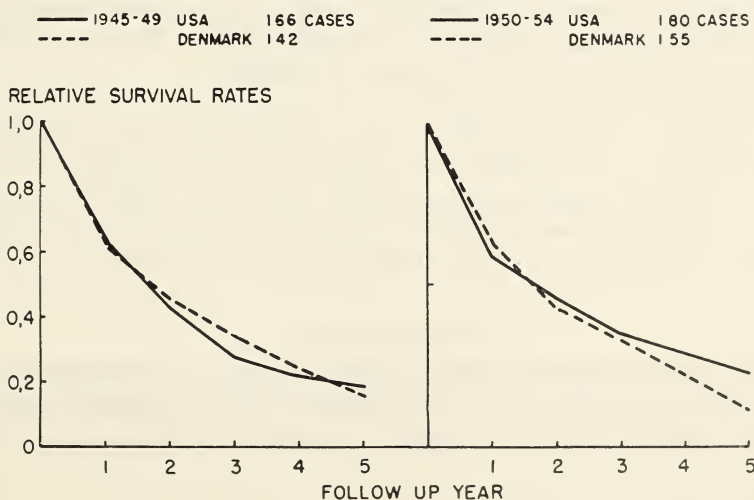


TEXT-FIGURE 1.—Chronic lymphatic leukemia in the United States and Denmark. Males 10-98 years. Total treated and untreated cases.

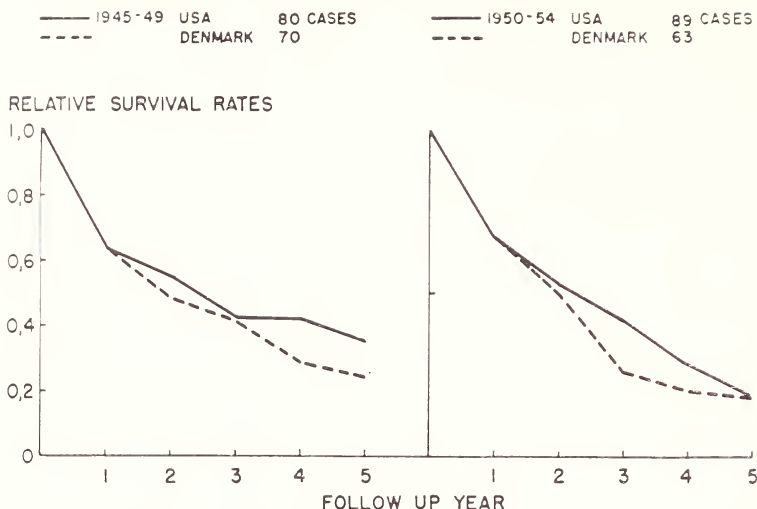


TEXT-FIGURE 2.—Chronic lymphatic leukemia in the United States and Denmark. Females 10-98 years. Total treated and untreated cases.

Although the curves may show some slightly more favorable survival rates after the first year, the final results seem much alike. Still the figures from the United States are slightly more favorable than those from Denmark. Since this applies both to cases treated and those not treated, the question arises whether we are dealing with exactly the same disease. The results for women in both countries are essentially alike.



TEXT-FIGURE 3.—Chronic lymphatic leukemia in the United States and Denmark. Males 10-98 years. Irradiation with or without chemotherapy and hormones.



TEXT-FIGURE 4.—Chronic lymphatic leukemia in the United States and Denmark. Females 10-98 years. Irradiation with or without chemotherapy and hormones.

### Chronic Myeloid Leukemia

The similarity between the United States and Denmark is closer for the chronic myeloid leukemia and so are the final results. This applies equally to treated and untreated cases. Results are generally less favorable than for chronic lymphatic leukemia.

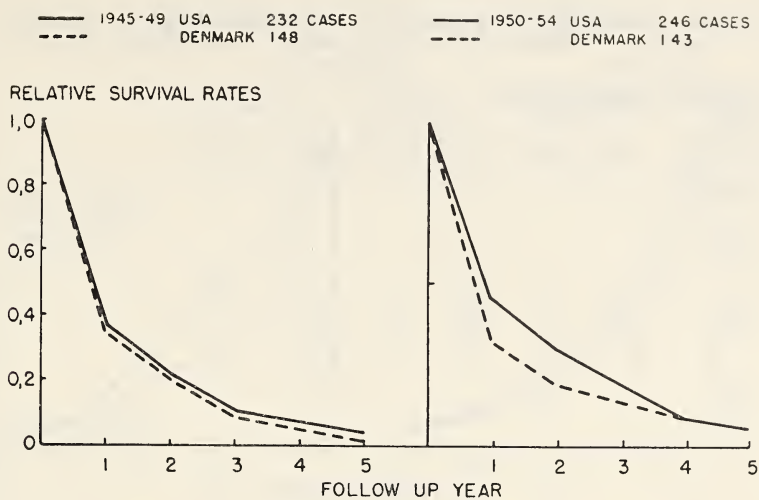
It should be noted that there were many more men with chronic lymphatic leukemia than with the chronic myeloid type. Therapeutic results are very much the same for both males and females.

Tables 1 through 12 show, although not apparent from the curve in the text-figures, that the combined treatment with radiation and chemotherapy plus hormones gives slightly better survival rates for the first few years than chemotherapy plus hormones alone. However, the absolute figures are so small that these results may be doubted because no definite information is available as to chemotherapeutic agent or hormones applied.

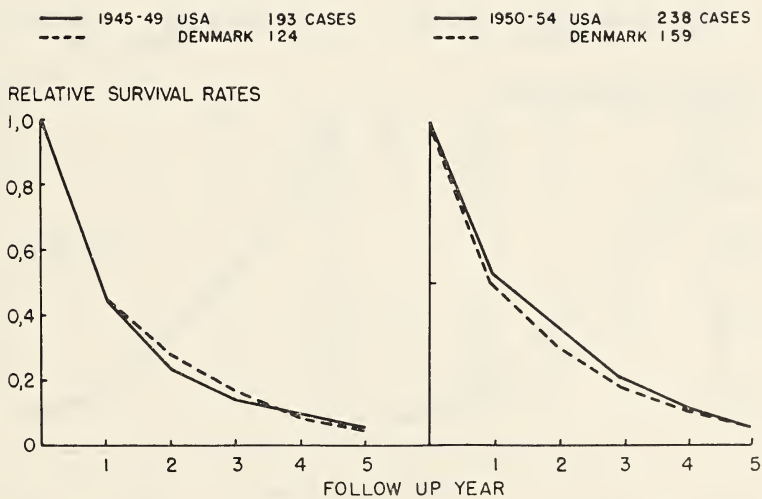
### Acute Leukemia

For acute leukemia we shall refer to tables only. This material shows a survival after 1 year of but 10 to 20 percent, but in consideration of the small numbers involved it is scarcely permissible to draw conclusions.

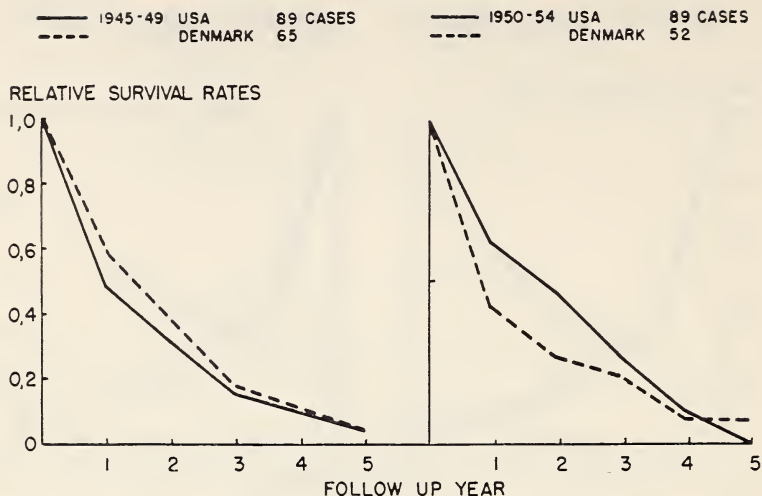




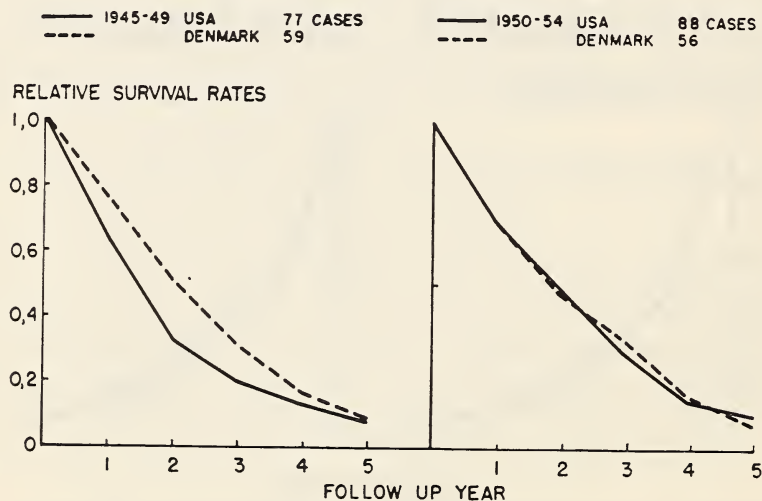
TEXT-FIGURE 5.—Chronic myeloid leukemia in the United States and Denmark. Males 10-98 years. Total treated and untreated cases.



TEXT-FIGURE 6.—Chronic myeloid leukemia in the United States and Denmark. Females 10-98 years. Total treated and untreated cases.



TEXT-FIGURE 7.—Chronic myeloid leukemia in the United States and Denmark. Males 10-98 years. Irradiation with or without chemotherapy and hormones.



TEXT-FIGURE 8.—Chronic myeloid leukemia in the United States and Denmark. Females 10-98 years. Irradiation with or without chemotherapy and hormones.

TABLE 1.—Acute leukemias, males 10–98 years, United States and Denmark

	United States				Denmark			
	1945–49		1950–54		1945–49		1950–54	
	Cases	Rates	Cases	Rates	Cases	Rates	Cases	Rates
<b>Irradiation with or without chemotherapy and hormones</b>								
(yrs)								
0–1	54	0.09	34	0.09	14	0.14	14	0.21
1–2	5	.05	3	.06	2	.07	3	.14
2–3	3	.02	2	.00	1	.07	2	.07
3–4	1	.02	—	—	1	.00	1	.00
4–5	1	.02	—	—	—	—	—	—
<b>Chemotherapy plus hormones only</b>								
(yrs)								
0–1	30	.03	123	.12	—	—	—	—
1–2	1	.00	14	.05	—	—	—	—
2–3	—	—	6	.02	—	—	—	—
3–4	—	—	2	.01	—	—	—	—
4–5	—	—	1	.01	—	—	—	—
<b>Any surgery</b>								
(yrs)								
0–1	22	.05	—	—	1	.00	3	.33
1–2	1	.00	—	—	—	—	1	.33
2–3	—	—	—	—	—	—	1	.00
3–4	—	—	—	—	—	—	—	—
4–5	—	—	—	—	—	—	—	—
<b>No known treatment</b>								
(yrs)								
0–1	140	.01	161	.10	57	.00	113	.01
1–2	2	.01	15	.04	—	—	1	.00
2–3	1	.01	6	.01	—	—	—	—
3–4	1	.01	2	.01	—	—	—	—
4–5	1	.01	2	.01	—	—	—	—
<b>Total treated and untreated</b>								
(yrs)								
0–1	246	.04	318	.10	72	.03	130	.04
1–2	9	.02	32	.05	2	.01	5	.02
2–3	4	.01	14	.02	1	.01	3	.01
3–4	2	.01	4	.02	1	.00	1	.00
4–5	2	.01	3	.01	—	—	—	—

TABLE 2.—Acute leukemias, females 10–98 years, United States and Denmark

	United States				Denmark			
	1945–49		1950–54		1945–49		1950–54	
	Cases	Rates	Cases	Rates	Cases	Rates	Cases	Rates
Irradiation with or without chemotherapy and hormones								
(yrs)								
0–1	23	0.09	28	0.11	5	0.20	10	0.00
1–2	2	.05	3	.11	1	.20	—	
2–3	1	.05	3	.04	1	.20	—	
3–4	1	.05	1	.04	1	.20	—	
4–5	1	.05	1	.04	1	.20	—	
Chemotherapy and hormones only								
(yrs)								
0–1	18	.11	102	.08	—		—	
1–2	2	.00	8	.04	—		—	
2–3	—		4	.01	—		—	
3–4	—		1	.01	—		—	
4–5	—		1	.01	—		—	
Any surgery								
(yrs)								
0–1	10	.00	3	.00	—		—	
1–2	—		—		—		—	
2–3	—		—		—		—	
3–4	—		—		—		—	
4–5	—		—		—		—	
No known treatment								
(yrs)								
0–1	106	.04	157	.11	27	.04	85	.01
1–2	4	.03	17	.03	1	.04	1	.01
2–3	3	.02	5	.01	1	.04	1	.01
3–4	2	.02	1	.01	1	.04	1	.01
4–5	2	.02	1	.01	1	.04	1	.01
Total treated and untreated								
(yrs)								
0–1	157	.05	290	.10	32	.06	95	.01
1–2	8	.03	28	.04	2	.06	1	.01
2–3	4	.02	12	.01	2	.06	1	.01
3–4	3	.02	3	.01	2	.06	1	.01
4–5	3	.02	3	.01	2	.06	1	.01



TABLE 3.—Acute leukemia, males and females 10-98 years, Finland, Norway, and Denmark

	Males				Females			
	Finland and Norway 1953-56		Finland, Norway, and Denmark 1950-56*		Finland and Norway 1953-56		Finland, Norway, and Denmark 1950-56*	
	Cases	Rates	Cases	Rates	Cases	Rates	Cases	Rates
Irradiation with or without chemotherapy and hormones								
(yrs)								
0-1	12	0.25	26	0.23	3	0.69	13	0.15
1-2	3	.00	6	.08	2	.70	2	.15
2-3	—		2	.04	2	.00	2	.00
3-4	—		1	.00	—		—	
4-5	—		—		—		—	
Chemotherapy and hormones only								
(yrs)								
0-1	184	.05	184	.05	123	.04	123	.04
1-2	9	.02	9	.02	5	.02	5	.02
2-3	3	.01	3	.01	2	.02	2	.02
3-4	2	.00	2	.00	2	.00	2	.00
4-5	—		—		—		—	
Any surgery								
(yrs)								
0-1	3	.00	6	.17	1	.00	1	.00
1-2	—		1	.17	—		—	
2-3	—		1	.00	—		—	
3-4	—		—		—		—	
4-5	—		—		—		—	
No known treatment								
(yrs)								
0-1	117	.01	230	.01	118	.02	203	.02
1-2	1	.00	2	.00	2	.01	3	.02
2-3	—		—		1	.01	2	.02
3-4	—		—		1	.00	2	.01
4-5	—		—		—		1	.00
Total treated and untreated								
(yrs)								
0-1	316	.04	446	.04	245	.04	340	.03
1-2	13	.01	18	.01	9	.02	10	.02
2-3	3	.01	6	.00	5	.01	6	.01
3-4	2	.00	3	.00	3	.00	4	.00
4-5	—		—		—		1	.00

\*Finland and Norway 1953-56, Denmark 1950-54.

TABLE 4.—Chronic lymphatic leukemia, males 10-98 years, United States and Denmark

	United States				Denmark			
	1945-49		1950-54		1945-49		1950-54	
	Cases	Rates	Cases	Rates	Cases	Rates	Cases	Rates
Irradiation with or without chemotherapy and hormones								
(yrs)								
0-1	166	0.65	180	0.60	142	0.61	155	0.63
1-2	103	.42	104	.46	84	.45	95	.43
2-3	65	.28	77	.36	62	.34	63	.33
3-4	42	.21	58	.30	45	.24	47	.22
4-5	30	.18	47	.23	31	.16	30	.11
Chemotherapy and hormones only								
(yrs)								
0-1	22	.70	51	.49	—	—	—	—
1-2	15	.38	24	.40	—	—	—	—
2-3	8	.39	19	.31	—	—	—	—
3-4	8	.35	14	.28	—	—	—	—
4-5	7	.16	12	.17	—	—	—	—
Any surgery								
(yrs)								
0-1	10	.51	5	.61	2	.51	10	.71
1-2	5	.53	3	.42	1	.53	7	.62
2-3	5	.44	2	.21	1	.00	6	.53
3-4	4	.45	1	.21	—	—	5	.33
4-5	4	.46	1	.21	—	—	3	.22
No known treatment								
(yrs)								
0-1	161	.41	220	.57	153	.27	174	.32
1-2	63	.33	121	.46	40	.17	54	.20
2-3	49	.28	92	.39	28	.12	33	.11
3-4	39	.22	71	.31	19	.10	18	.07
4-5	31	.13	53	.26	16	.06	11	.05
Total treated and untreated								
(yrs)								
0-1	359	.53	456	.58	297	.43	339	.47
1-2	186	.38	252	.46	125	.30	156	.32
2-3	127	.29	190	.36	91	.22	102	.23
3-4	93	.23	144	.30	64	.17	70	.15
4-5	72	.17	113	.23	47	.11	44	.09

TABLE 5.—Chronic lymphatic leukemia, females 10-98 years, United States and Denmark

	United States				Denmark			
	1945-49		1950-54		1945-49		1950-54	
	Cases	Rates	Cases	Rates	Cases	Rates	Cases	Rates
<b>Irradiation with or without chemotherapy and hormones</b>								
(yrs)								
0-1	80	0.63	89	0.68	70	0.64	63	0.67
1-2	49	.50	59	.52	44	.48	41	.40
2-3	38	.37	44	.41	34	.34	24	.26
3-4	27	.37	31	.27	23	.29	15	.20
4-5	26	.31	19	.18	19	.24	11	.17
<b>Chemotherapy and hormones only</b>								
(yrs)								
0-1	6	.34	43	.47	—		—	
1-2	2	.35	20	.39	—		—	
2-3	2	.36	16	.36	—		—	
3-4	2	.37	14	.21	—		—	
4-5	2	.38	8	.19	—		—	
<b>Any surgery</b>								
(yrs)								
0-1	10	.40	4	.51	4	.76	10	.91
1-2	4	.21	2	.52	3	.77	9	.72
2-3	2	.21	2	.53	3	.53	7	.62
3-4	2	.21	2	.54	2	.54	6	.52
4-5	2	.21	2	.28	2	.55	5	.53
<b>No known treatment</b>								
(yrs)								
0-1	90	.41	122	.64	81	.33	105	.44
1-2	36	.33	75	.54	26	.27	46	.33
2-3	28	.33	61	.50	21	.22	33	.29
3-4	27	.27	54	.45	15	.22	28	.26
4-5	21	.20	46	.38	15	.15	24	.23
<b>Total treated and untreated</b>								
(yrs)								
0-1	186	.50	258	.62	155	.49	178	.55
1-2	91	.40	156	.51	73	.34	96	.38
2-3	70	.34	123	.44	58	.24	64	.30
3-4	58	.31	101	.35	40	.23	49	.26
4-5	51	.25	75	.27	36	.18	40	.23

TABLE 6.—Chronic lymphatic leukemia, males and females 10-98 years, Finland, Norway, and Denmark

	Males				Females			
	Finland and Norway 1953-56		Finland, Norway, and Denmark 1950-56*		Finland and Norway 1953-56		Finland, Norway, and Denmark, 1950-56*	
	Cases	Rates	Cases	Rates	Cases	Rates	Cases	Rates
Irradiation with or without chemotherapy and hormones (yrs)								
0-1	57	0.55	212	0.61	38	0.76	101	0.70
1-2	30	.30	125	.40	28	.51	69	.44
2-3	16	.18	79	.29	18	.43	42	.32
3-4	9	.10	56	.19	15	.35	30	.26
4-5	5	.04	35	.10	12	.18	23	.18
Chemotherapy and hormones only (yrs)								
0-1	82	.54	82	.54	43	.51	43	.51
1-2	43	.41	43	.41	21	.38	21	.38
2-3	31	.34	31	.34	15	.34	15	.34
3-4	25	.24	25	.24	13	.24	13	.24
4-5	16	.18	16	.18	7	.22	7	.22
Any surgery (yrs)								
0-1	6	.84	16	.76	2	.00	12	.76
1-2	5	.85	12	.71	—		9	.60
2-3	5	.86	11	.66	—		7	.52
3-4	5	.34	10	.34	—		6	.44
4-5	2	.34	5	.28	—		5	.44
No known treatment (yrs)								
0-1	50	.40	224	.34	30	.62	135	.48
1-2	19	.24	73	.21	18	.46	64	.36
2-3	11	.18	44	.12	13	.36	46	.31
3-4	8	.14	26	.08	10	.19	38	.25
4-5	5	.14	16	.07	5	.08	29	.20
Total treated and untreated (yrs)								
0-1	195	.52	534	.48	113	.61	291	.58
1-2	97	.35	253	.32	67	.44	163	.40
2-3	63	.27	165	.24	46	.38	110	.33
3-4	47	.18	117	.16	38	.27	87	.26
4-5	28	.14	72	.10	24	.16	64	.20

\*Finland and Norway 1953-56, Denmark 1950-54.



TABLE 7.—Chronic myeloid leukemia, males 10–98 years, United States and Denmark

	United States				Denmark			
	1945–49		1950–54		1945–49		1950–54	
	Cases	Rates	Cases	Rates	Cases	Rates	Cases	Rates
Irradiation with or without chemotherapy and hormones								
(yrs)								
0–1	89	0.47	89	0.66	65	0.59	52	0.43
1–2	41	.28	57	.50	38	.39	21	.27
2–3	24	.14	42	.28	25	.18	13	.21
3–4	12	.07	23	.11	11	.11	10	.08
4–5	6	.04	9	.05	7	.05	4	.08
Chemotherapy and hormones only								
(yrs)								
0–1	8	.64	45	.48	—		—	
1–2	5	.26	21	.24	—		—	
2–3	2	.13	10	.17	—		—	
3–4	1	.00	7	.08	—		—	
4–5	—		3	.05	—		—	
Any surgery								
(yrs)								
0–1	10	.63	—		1	.00	2	1.00
1–2	6	.18	—		—		2	.51
2–3	1	.00	—		—		1	.00
3–4	—		—		—		—	
4–5	—		—		—		—	
No known treatment								
(yrs)								
0–1	125	.25	112	.31	82	.14	89	.25
1–2	30	.16	33	.20	11	.07	22	.14
2–3	19	.11	20	.13	5	.04	12	.11
3–4	12	.07	12	.09	3	.01	9	.10
4–5	8	.05	8	.07	1	.00	8	.06
Total treated and untreated								
(yrs)								
0–1	232	.36	246	.47	148	.34	143	.32
1–2	82	.21	111	.31	49	.20	45	.19
2–3	46	.12	72	.19	30	.09	26	.14
3–4	25	.07	42	.09	14	.05	19	.09
4–5	14	.05	20	.06	8	.02	12	.06

TABLE 8.—Chronic myeloid leukemia, females 10–98 years, United States and Denmark

	United States				Denmark			
	1945–49		1950–54		1945–49		1950–54	
	Cases	Rates	Cases	Rates	Cases	Rates	Cases	Rates
Irradiation with or without chemotherapy and hormones								
(yrs)								
0–1	77	0.60	88	0.70	59	0.75	56	0.69
1–2	45	.31	60	.51	44	.50	38	.48
2–3	22	.17	42	.31	29	.31	26	.34
3–4	12	.11	25	.16	18	.17	18	.17
4–5	8	.07	13	.11	10	.09	9	.08
Chemotherapy and hormones only								
(yrs)								
0–1	18	.62	36	.37	—		—	
1–2	11	.57	13	.17	—		—	
2–3	10	.29	6	.17	—		—	
3–4	5	.23	6	.11	—		—	
4–5	4	.12	4	.00	—		—	
Any surgery								
(yrs)								
0–1	9	.00	2	.00	2	.05	6	.67
1–2	—		—		1	.00	4	.51
2–3	—		—		—		3	.51
3–4	—		—		—		3	.34
4–5	—		—		—		2	.17
No known treatment								
(yrs)								
0–1	89	.29	112	.47	63	.15	97	.38
1–2	25	.13	51	.31	10	.07	36	.19
2–3	11	.08	33	.17	5	.04	18	.05
3–4	7	.06	18	.11	3	.01	5	.04
4–5	5	.04	11	.05	1	.01	4	.03
Total treated and untreated								
(yrs)								
0–1	193	.33	238	.53	124	.45	159	.50
1–2	81	.24	124	.36	55	.28	78	.31
2–3	43	.14	81	.22	34	.17	47	.18
3–4	24	.10	49	.13	21	.09	26	.11
4–5	17	.06	28	.06	11	.05	15	.06

TABLE 9.—Chronic myeloid leukemia, males and females 10–98 years, Finland, Norway, and Denmark

	Males				Females			
	Finland and Norway 1953–56		Finland, Norway, and Denmark 1950–56*		Finland and Norway 1953–56		Finland, Norway, and Denmark 1950–56*	
	Cases	Rates	Cases	Rates	Cases	Rates	Cases	Rates
<b>Irradiation with or without chemotherapy and hormones</b>								
(yrs)								
0–1	49	0.56	101	0.49	49	0.66	105	0.67
1–2	27	.30	48	.27	32	.49	70	.47
2–3	14	.24	27	.21	23	.28	49	.30
3–4	11	.22	21	.14	13	.11	31	.14
4–5	10	.22	14	.14	4	.06	13	.07
<b>Chemotherapy and hormones only</b>								
(yrs)								
0–1	97	.33	97	.33	103	.35	103	.35
1–2	31	.21	31	.21	35	.26	35	.26
2–3	20	.14	20	.14	25	.18	25	.18
3–4	13	.09	13	.09	17	.10	17	.10
4–5	7	.07	7	.07	9	.08	9	.08
<b>Any surgery</b>								
(yrs)								
0–1	5	.00	7	.30	7	.43	13	.55
1–2	—		2	.15	3	.43	7	.47
2–3	—		1	.00	3	.29	6	.39
3–4	—		—		2	.15	5	.23
4–5	—		—		—		2	.12
<b>No known treatment</b>								
(yrs)								
0–1	61	.29	150	.27	62	.16	159	.30
1–2	17	.14	39	.14	10	.10	46	.16
2–3	8	.12	20	.11	6	.07	24	.06
3–4	7	.07	16	.08	4	.05	9	.05
4–5	4	.04	12	.04	3	.05	7	.04
<b>Total treated and untreated</b>								
(yrs)								
0–1	212	.36	355	.35	221	.37	380	.43
1–2	75	.20	120	.20	80	.26	158	.28
2–3	42	.15	68	.15	57	.16	104	.17
3–4	31	.11	50	.10	36	.08	62	.09
4–5	21	.09	33	.08	16	.06	31	.06

\*Finland and Norway 1953–56, Denmark 1950–54.

TABLE 10.—Acute and chronic leukemias, males and females, 0-9 years

		Cases					
		Males			Females		
		Total	Percent of all ages	Rates of 1st year	Total	Percent of all ages	Rates of 1st year
Acute leukemias							
United States	1945-49	101	29.1	0.03	87	35.6	0.03
	1950-54	147	31.6	.20	143	33.0	.13
Denmark	1945-49	38	34.5	.00	32	32.3	.06
	1950-54	56	30.1	.05	37	28.0	.06
Finland	1953-56	64	36.6	.02	40	31.7	.05
Norway	1953-56	61	22.9	.13	61	27.7	.08
Chronic lymphatic leukemia							
United States	1945-49	54	13.1	.04	39	17.3	.08
	1950-54	37	7.5	.14	25	8.8	.12
Denmark	1945-49	23	7.2	.00	28	15.3	.04
	1950-54	24	6.6	.04	15	7.8	.07
Finland	1953-56	9	9.6	.11	4	6.9	.00
Norway	1953-56	1	0.9	1.00	—	—	—
Chronic myeloid leukemia							
United States	1945-49	9	3.7	0.11	6	3.0	0.00
	1950-54	9	3.5	.22	7	2.9	.15
Denmark	1945-49	10	6.3	.00	14	10.1	.14
	1950-54	6	4.0	.17	3	1.9	.00
Finland	1953-56	8	8.9	.13	4	4.0	.00
Norway	1953-56	1	0.8	.00	2	1.6	.00

TABLE 11.—Acute leukemias, both sexes, all ages, France 1945-1959

	Cases	Rates
Irradiation		
(yrs)		
0-1	79	0.50
1-2	35	.43
2-3	24	.29
3-4	10	.26
4-5	5	.20
Other treatment		
(yrs)		
0-1	94	.24
1-2	14	.16
2-3	8	.12
3-4	6	.10
4-5	4	.10
Total		
(yrs)		
0-1	173	.36
1-2	49	.29
2-3	32	.20
3-4	16	.17
4-5	9	.16



TABLE 12.—Chronic leukemias, both sexes, all ages, France 1945–1959

	Chronic lymphatic leukemia		Chronic myeloid leukemia	
	Cases	Rates	Cases	Rates
Irradiation				
(yrs)				
0–1	150	0.67	205	0.60
1–2	91	.50	113	.45
2–3	59	.42	75	.27
3–4	40	.33	34	.19
4–5	24	.24	15	.11
Other treatment				
(yrs)				
0–1	49	.53	46	.63
1–2	23	.38	22	.43
2–3	16	.31	13	.25
3–4	11	.25	6	.26
4–5	7	.26	1	.26
Total				
(yrs)				
0–1	199	.63	251	.60
1–2	114	.47	135	.45
2–3	75	.39	88	.26
3–4	51	.31	40	.19
4–5	31	.25	16	.12



## Factors Influencing Survival Time in Patients With Acute Leukemia

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THE purpose of this investigation was the study of the general, clinical, cytological, and hematological factors that may influence the survival of patients with acute leukemia who were treated with the usual antileukemic drugs.

### MATERIAL AND METHODS

*Patient sample.*—Of 345 cases of acute leukemia (AL), diagnosed from January, 1959, to December, 1961, in the Department of Hematology, Hôpital Saint-Louis, 89 cases had to be eliminated because of inadequate follow-up; 256 cases remained for analysis. The onset of the disease was fixed as the date on which the first hematological examination was indisputably designated as leukemia.

*Cytological classification.*—All patients were diagnosed by repeated peripheral blood and bone marrow smears, stained with May-Grünwald-Giemsa.

The cytological classification was achieved after several observers had examined the slides, using morphological criteria described in a previous study (1).

All cases were distributed into 2 cytological groups: 135 acute lymphoblastic leukemia (ALL) and 121 acute myeloblastic leukemia (AML).

The ALL group is homogeneous; the malignant cell in every instance is the lymphoblast, alone or associated with a small number of less-differentiated cells.

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<sup>2</sup> The authors wish to express their thanks to Mrs. Lecuyer for her most valuable assistance.

The AML group is more complex. The observations were divided as follows:

- 95 *typical AML*.—These are characterized by pure myeloblastic proliferation or associated in various proportions with undifferentiated or monocytoid elements.
- 14 *acute promyelocytic leukemias*.—We included these with the AML, as do most authors, since the malignant cell belongs to the same cell line and seems close to the myeloblast.
- 9 *undifferentiated acute leukemias*.—Because of the characteristics of their nuclei and the marked basophilia of their cytoplasm, these malignant cells, although not containing any granulations, seem very close to the early myelogenous cells and were classified as such.
- 3 *so-called "monoblastic" leukemias*.—Since these malignant "monoblasts" are not readily distinguished from myeloblasts or sometimes are associated with them, we thus assigned these cases to the myeloblastic leukemias.

*Therapeutic schedule*.—All patients were treated alike. Prednisone (3 mg/kg/day) and amethopterin (0.15 mg/kg/day) were given as initial treatment and 6-mercaptopurine (2.5 mg/kg/day) as maintenance treatment. Antibiotics and transfusions were given as required.

## RESULTS

### *Comparative Study of the Two Types of Acute Leukemia*

From the data summarized in table 1, the following points are emphasized:

The average ages of the patients were significantly different in the two cytological types (ALL, 13.8 years; AML, 30.7 years;  $P = 10^{-3}$ ). The difference distribution in the clinical signs in the two classes of leukemia is statistically significant. The major difference is the marked variation in survival time between the two types of leukemia (mean survival duration: ALL = 11.6 months; AML = 4.3 months;  $P = 10^{-3}$ ). This difference (text-fig. 1) is explained by the higher incidence of complete remissions under treatment in ALL than in AML (ALL: 64%; AML: 14%;  $P = 10^{-3}$ ).

The cytological type is such an important one that any other factors which may modify the survival time should be estimated in each cytological group separately.

### *Factors Influencing the Survival Time in ALL and AML*

Tables 2 and 3 show the following results:

(a) There is a slight correlation between age and survival time in ALL, the survival time being shorter in adults over 30. In AML, such a relationship is not apparent.

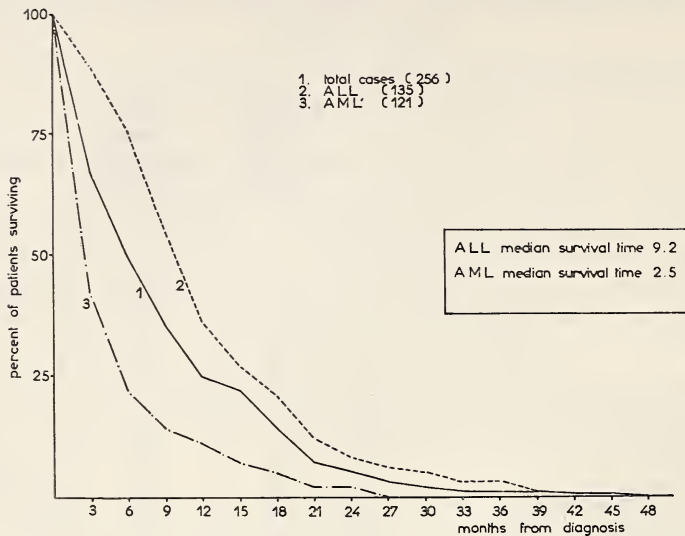


TABLE 1.—Comparative study of principal features in acute lymphoblastic and myeloblastic leukemias

Features	Acute lymphoblastic leukemia, 135 cases (%)	Acute myeloblastic leukemia, 121 cases (%)	Significance
Age (years)			
Under 10	52	14	$P = 0.001$
10-19	28	26	
20-29	6	16	
30 and over	14	44	
Males	53	55	
Females	47	45	
Patients with:			
Hemorrhages	55	67	$P = 0.01$
Skeleton involvement	40	22	
Splenomegaly	57	36	$P = 0.001$
Lymph node involvement	58	39	$P = 0.01$
Gum infiltration	3	20	$P = 0.001$
Meningeal involvement	16	4	
Extrahematopoietic tumors	8	4	
Patients with:			
RBC $10^6/\text{mm}^3$	$<2$ 21 $2-3.5$ 58 $>3.5$ 20	20 70 10	
Platelets $10^3/\text{mm}^3$	$<100$ 67 100-200 18 $>200$ 15	77 17 6	
WBC $10^3/\text{mm}^3$	$<5$ 29 6-50 43 51-100 13 $>100$ 14	25 47 11 17	
Leukemic cells $10^3/\text{mm}^3$	$<5$ 49 5-50 28 51-100 11 $>100$ 11	41 35 9 15	
Infiltration of the bone marrow by leukemic cells $>75\%$	83	75	
Mean survival duration (months)	11.6	4.3	$P = 0.001$
Percent of complete remissions (1 or more)	64	14	$P = 0.001$

(b) Hemorrhages present at the onset of the disease were of some value for the prognosis. The other clinical signs were of no value for estimation of the prognosis.

(c) The survival duration appears longer in patients with ALL who have meningeal involvement than in those without this complication. This can be explained by the long mean time from the onset of systemic leukemia to the onset of the meningitis (14.4 months). Therefore,



TEXT-FIGURE 1.—Survival curves of patients with acute leukemia according to the cytological type.

meningeal involvements are observed mainly in patients with leukemias of long duration.

(d) The initial white blood cell and leukemic blood cell count are moderately correlated with survival; the survival is shorter in patients with very high leukocytosis.

(e) The degree of infiltration of the bone marrow by the leukemic cells is correlated with survival; the survival is shorter when the percentage of leukemic cells in the bone marrow smears is over 75.

(f) The most important result of this study is that, for the two groups with ALL, there is a very high correlation between platelet count and survival. The patients without initial thrombopenia have a much longer survival time than the others. In ALL, the survival time is 9.5 months in patients with 100,000 platelets per  $\text{mm}^3$  or less and 19.9 months in those with 200,000 platelets per  $\text{mm}^3$  or more;  $P = 10^{-3}$ . In AML, the survival time is 2.7 months in patients with 100,000 platelets per  $\text{mm}^3$  or less and 14.0 months in those with 200,000 platelets per  $\text{mm}^3$  or more;  $P = 10^{-3}$ .

(g) Hemorrhages are often associated with a low platelet count, and thus the question arises as to whether each factor acts independently in survival time. Table 4 shows that for ALL, hemorrhages do not seem to play an independent role, whereas the platelet count is of definite value in survival time. In AML, the two factors seem to have autonomous roles, but the sample numbers are small and complementary studies are necessary.

TABLE 2.—Factors influencing the survival time in acute lymphoblastic leukemia\*

	Age				Sex		Hemorrhages		Skeleton involvement		Splenomegaly		Lymph node involvement		Gum infiltration		Meningeal involvement		Extrahematopoietic tumors		
	<5	5-9	10-19	20-29	>30	M	F	+	-	+	-	+	-	+	-	+	-	+	-		
Number of cases	42	28	38	8	19	71	64	66	53	48	71	68	51	69	50	4	115	21	114	11	124
Survival time (months)	12.6	11.8	13.0	13.7	5.6	12.1	11.1	10.1	13.9	10.7	12.6	10.8	13.1	12.0	11.5	7.0	12.0	18.2	10.4	20.5	10.8
Significance	$P = 0.05$						$P = 0.05$										$P = 0.001$				
	RBC $10^9/\text{mm}^3$				Platelets $10^9/\text{mm}^3$				WBC $10^9/\text{mm}^3$				Leukemic cells $10^9/\text{mm}^3$				Total infiltration of the bone marrow by leukemic cells $>75\%$				
	<2	2-3.5	>3.5		<100	100-200	>200		<5	5-50	51-100	>100	<5	5-50	51-100	>100	+	-			
Number of cases†	22	60	21		71	19	16		31	46	14	15	52	30	12	12	88	18			
Survival time (months)	8.7	11.3	16.6		9.5	12.9	19.9		15.1	11.4	8.8	8.5	13.2	11.8	6.9	9.6	10.6	17.3			
Significance	$P = 0.05$				$P = 0.001$								$P = 0.01$								

\*Only when they appeared at the onset of the disease are these factors recorded (except for meningitis). Of 135 patients, 16 were not seen by us at the onset of the disease; these cases have not been included in this table as far as hemorrhages, skeleton involvement, splenomegaly, lymph node involvement, or gum infiltration are concerned.

†The number of cases is lower because patients who had been treated for a short time before examination were excluded.

TABLE 3.—Factors influencing the survival time in acute myeloblastic leukemia \*

	Age				Sex		Hemorrhages		Skeleton involvement	Splenomegaly		Lymph node involvement	Gum infiltration		Meningeal involvement	Extramedullary poietic tumors				
	<10	10-19	20-29	>30	M	F	+	-	+	-	+	-	+	-	+	-				
Number of cases	17	31	20	53	67	54	76	38	25	89	41	73	44	70	23	91	5	116		
Survival time (months)	3.8	5.8	4.0	3.7	4.1	4.6	2.7	6.3	4.6	3.7	3.6	4.0	3.3	4.2	2.6	4.2	10.5	4.1	13.3	4.0
Significance	$P = 0.001$																			

	RBC $10^9/\text{mm}^3$			Platelets $10^9/\text{mm}^3$			WBC $10^9/\text{mm}^3$			Leukemic cells $10^9/\text{mm}^3$			Total infiltration of the bone marrow by leukemic cells >75%					
	<2	2-3.5	>3.5	<100	100-200	>200	<5	5-50	51-100	>100	<5	5-50		51-100	>100			
Number of cases†	18	63	9	80	18	6	26	49	11	18	43	36	9	16	78	26		
Survival time (months)	2.5	3.2	5.0	2.7	4.1	14.0	5.2	3.8	1.9	1.9	5.2	3.0	1.6	1.9	3.0	5.5		
Significance	$P = 0.001$												$P = 0.05$			$P = 0.02$		

\*Only when they appeared at the onset of the disease are these factors recorded (except for meningitis). Of 121 patients, 7 were not seen by us at the onset of the disease; these cases have not been included in this table as far as hemorrhages, skeleton involvement, splenomegaly, lymph node involvement, or gum infiltration are concerned.

†The number of cases is lower because patients who had been treated for a short time before examination were excluded.



TABLE 4.—Comparative study of the role of hemorrhages and thrombocytopenia in survival time\*

Acute lymphoblastic leukemia						
		Hemorrhages				Significance
		—		+		
Platelet count 10 <sup>3</sup> /mm <sup>3</sup>	<100	10. 5	(21)	9. 1	(49)	$P = 0. 05$
	100–200	14. 4	(11)	11. 0	(8)	
	>200	20. 7	(12)	17. 5	(4)	
Significance	$P = 0. 05$					
Acute myeloblastic leukemia						
		Hemorrhages				Significance
		—		+		
Platelet count 10 <sup>3</sup> /mm <sup>3</sup>	<100	3. 9	(22)	2. 3	(57)	$P = 0. 05$
	100–200	6. 0	(7)	2. 8	(11)	
	>200	14. 0	(6)			
Significance	$P = 0. 01$					

\*Figures in parentheses indicate the number of patients.

## SUMMARY

A study of factors influencing the survival time in acute leukemia based on material from 256 similarly treated cases shows that:

(a) The cytological type is the most important factor, the average survival time being 11.6 months for ALL and 4.3 months for AML. This difference is so great that it requires the separation of acute leukemia into two main cytological types for any statistical or epidemiological work.

(b) The platelet count has a very important prognostic significance, the patients without initial thrombopenia having a much longer survival than the others.

(c) The white blood cell count has a moderate prognostic value.

(d) Age has some bearing on the survival in ALL, but not in AML.

## REFERENCE

- (1) BERNARD, J. BOIRON, M., WEIL, M., LEVY, J. P., SELIGMANN, M., and NAJEAN, Y.: Etude de la rémission complète des leucémies aigües. N Rev Fr Hemat 2: 195, 1962.

## Summary of General Discussion

Analysis of the collected registry materials on survival rates of leukemia patients is difficult and inconclusive because of a serious lack of uniformity in the classification of various types of leukemia. Registries should cooperate in attempts to establish and use uniform criteria for classifying leukemia as acute or chronic and as myeloid, lymphatic, or other. There was some disagreement about the difficulty of distinguishing between the forms of leukemia, but none about the importance of doing so. Ways to ensure uniform application of any generally accepted criteria were not discussed.

The high proportion of cases tabulated as "no known treatment" may be misleading. Many of these patients did, in fact, have treatment that was either started after the 4-month interval used in the end-results tabulation to define first course of therapy, or which did not fall into one of the standard categories of surgery, radiation, hormones, or chemotherapy. It might be useful to establish a special treatment code for leukemia to permit classification of patients into meaningful therapeutic categories.

The low incidence and rapid course of leukemia, especially in humans under the age of 10 years, create difficult statistical problems that could be reduced by data pooled over longer periods or larger geographic areas and by a study of survival in terms of months rather than completed years.

The ordinary concept of tumor stage has little meaning in leukemia. However, various symptoms, physical signs, and laboratory observations of newly diagnosed cases can be helpful in the classification of the severity of the disease and in the prediction of its future course. In France, platelet counts have been especially helpful.

The complementary value of epidemiologic studies on all patients in defined populations and of detailed clinical studies on small or selected groups of patients is as apparent for leukemia as for other types of tumor.

It is not clear whether the observed increase in average survival time from the first cohort to the second in the end-results series is due to changes in the criteria for diagnosis or differentiation of various types of leukemia, diagnosis at an earlier stage of the disease, or the introduction of more effective treatment methods. Determination of the time from which survival should be measured may be very difficult.

Registry materials on cancer are used in many different ways, including epidemiologic studies, services to patients, and treatment evaluation. These various uses sometimes conflict, so that compromises are necessary in registry codes and procedures.

## **Appendix**

Some Observations Concerning Comparability in These Data. WILLIAM I.  
LOURIE, JR., USA

Computation of Survival Rates

Survival Tables

These data were presented at the International Symposium on End Results  
of Cancer Therapy, Sandefjord, Norway, September 16-20, 1963.





## Some Observations Concerning Comparability in These Data<sup>1</sup>

WILLIAM I. LOURIE, JR., *Biometry Branch,  
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THE attempt to compare data from different countries concerning the treatment of cancer patients and the end results of treatment was a pioneering effort. It is, therefore, useful to examine some of the specific problems of comparability that were encountered as indicative of possible approaches to make future comparisons more meaningful.

### I. SYSTEMS OF DATA COLLECTION AND AGREED RESTRICTION OF TABULATIONS

#### A. Confirmed Versus Unconfirmed Cases

Initially the Ad Hoc Group decided to limit its study to the comparison of end results of histologically confirmed cancer cases. However, during the discussions in London in the spring of 1962, the observation was made that there was great variation from country to country in the proportion of cancer cases which were histologically confirmed. Lung, prostate, and most digestive tract sites presented great contrasts. In some countries there were as many unconfirmed as confirmed cases; in other countries the relative number of unconfirmed cases was very low. Thus, looking only at the end results of confirmed cases might not produce a fair appraisal of the usual success in treatment of cancer cases and would probably bias country-to-country comparisons. Therefore, in planning for this Symposium in Sandefjord, it was decided that data for unconfirmed cases should also be assembled. To provide the greatest utility for the

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<sup>1</sup>This paper was originally presented at the opening session of the Symposium. This fact helps explain why discussants of the various papers often stated that no definitive conclusions could be drawn from the available end results data.

<sup>2</sup>National Institutes of Health, Public Health Service, U.S. Department of Health, Education, and Welfare.

analysts, data for confirmed and unconfirmed cases were to be tabulated separately, as well as in combination.

### B. The "Death Certificate Only" Case

There is another problem in comparability which also involves consideration of cancer data the Group had agreed not to examine. In its emphasis on evaluation of treatment, the Ad Hoc Group omitted from its planned studies the scrutiny of cancer cases reported *only* via the death certificate. If a cancer case is made known to a registry solely from the routine examination of death certificates, presumably the case has not been seen for cancer in a reporting hospital. (The registries here represented are essentially based upon reports from hospitals.) While such a person may or may not have received treatment, the treatment information on the death certificate is very imprecise. So also is the information concerning the date of diagnosis, the date of first treatment, and thus any estimate of survival time. It, therefore, seemed logical to omit such cases from any analysis of treatment and survival.

However, omission of such cases may affect the validity of the analysis of the survival experience of the total of all persons with a particular form of cancer in at least two ways:

- (a) contrast between countries which differ in the completeness of reporting of cancer cases, and
- (b) time-period comparisons for a single country which has had changes over time in the completeness of reporting.

As an example of the first type, let me point to some data from Norway and Connecticut concerning cancer of the colon and rectum. In the same time period, combining all the data, there were 5,817 cases from Connecticut defined according to the criteria for this Symposium; there were 4,185 comparable analytic cases from Norway. However, in Connecticut there were an additional 1,042 cases classified as "death certificate only," whereas in Norway there were but 42. "Death certificate only" cases represented an additional 18 percent in Connecticut but only an additional 1 percent in Norway.

One can easily understand how such differences can occur when one is informed that in Norway a query is directed to the medical practitioner who signed the death certificate if the case is not on file in the registry. The doctor's reply provides the opportunity to acquire some reports accidentally not submitted by certain hospitals. Even if the patient had not been treated in a hospital, the case is registered if the doctor's information is complete. In Connecticut, a query is made only to a hospital mentioned on the death certificate. (This is the present practice. However, for the years covered by the data being discussed, very few queries were made.) If no hospital is mentioned, no questionnaire is sent out. Thus, in Norway there is a checking procedure which should produce more

missing reports than in Connecticut. In Norway, also, there is the possibility of registering a physician's report on a nonhospitalized case.

What does this difference in collection practice do to the statistics on cancer survival? The survival rate for the total of reported cases in Connecticut tends to be biased upward in comparison with Norway. A sizable number of cases with approximately zero survival are excluded from the Connecticut data, whereas similar cases are included in the Norwegian data. It is also highly probable that when one examines subcategories of the data it will be found that this lack of comparability is not uniform. Its influence should vary with age, economic status, distance from a hospital, or whatever other cultural factors are associated with being differentially covered in the two systems.

Such lack of comparability should affect especially an analysis of the survival of those cancer patients receiving no treatment at all or receiving only symptomatic or supportive therapy at home. The proportion of all cancer patients represented by this group varies by site and over time. Differential coverage of such cases makes it necessary to interpret with extreme caution apparent differences in survival for the total of reported cases with otherwise well-defined common characteristics.

While contributing to a lack of precision in assessing survival of total groups or of "untreated" cases, this factor should not affect the analysis of treated patients nor the results of specific therapy. Furthermore, it seems plausible that the cases at issue would usually be in the last stages of the disease. Therefore, there should be no effect upon the interpretation of data on localized cases.

Should the Ad Hoc Group wish to base future studies on all the data available to the cooperating registries, Connecticut, Denmark, Finland, and Norway can provide information on the "death certificate only" cases. England and Wales could not in the past, but at present it is possible for the registry to get such information. Of the American registries whose data are included here, only Connecticut is population-based. Therefore, except in Connecticut, data on "death certificate only" cases just do not arise. The situation is essentially the same for the French registry which also does not cover a specified population.

From the two examples mentioned so far, the "unconfirmed" case and the "death certificate only" case, it seems clear that future studies should not *a priori* restrict the collection of data. In these pioneering collaborative studies an attempt should be made to collect information on *all* known cases of the cancer being investigated. The analyst can then decide how best to utilize the available data.

### C. The Proportion of Unstaged Cases

Another interesting problem in comparability between data from different countries arises from the varying proportion of cases which are "un-



staged." Again using data for cancer of the colon and of the rectum as an example, the following information is pertinent:

<i>Registry</i>	<i>Percent unstaged</i>
England and Wales	—
France	0
Denmark	3
U.S. Hospitals	6
Finland	8
U.S. Central	8
Norway	9
Connecticut	9

The figures range from 9 percent for Norway and Connecticut down to France with less than 1 percent and England without a single case. Examination of data for other sites indicates that this is not an atypical pattern among the different registries. Although there are differences according to sex and registry, it is not uncommon to find figures in excess of 15 percent for esophagus, stomach, and lung.

Unknown stage is found among both confirmed and unconfirmed cases. However, a much greater proportion of the unconfirmed cases are also classified as unstaged. For some sites approximately 40 percent of the unconfirmed cases are classified as stage unknown. There is, on the other hand, no direct association between the proportion of stage unknown cases and proportion of unconfirmed cases.<sup>3</sup>

It is most likely that the cases with unknown stage have not been reviewed as yet by many of the registries. It is probable that review would diminish the number. Possibly, the Group might find it desirable to set a standard such that there be no analysis by stage if the proportion of unstaged cases is higher than a specific figure.

Why is there such a variation by country in the proportion of registered patients for whom no stage is assigned? An attempt to answer this question will bring into the open some basic differences in the collection and coding systems. Some further details appear in Section II, Part D of this Appendix, but a summary here may be useful.

Several different situations occur in respect to the staging of those sites for which there is no internationally accepted classification scheme:

1. Information concerning stage was not collected heretofore. In the absence of such information, an approximation to a stage classification is derived by utilization of information concerning treatment. Radical treatment is coded as localized stage; palliative treatment is coded as a nonlocalized condition. Since treatment information is always available, there is no residue of cases to be coded as unknown stage. This classification is done at the registry office (Denmark, stomach).

<sup>3</sup> For the sites mentioned above (colon and rectum) Finland has approximately 40 percent unconfirmed cases; Norway, England, France, and Denmark approximately 30 percent unconfirmed; and the U.S. registries, including Connecticut, have about 10 percent unconfirmed cases.



2. Information is collected as to whether there is evidence or proof of lymph node involvement and/or metastases, but the reporting doctor is not asked for an assessment of clinical stage.

(a) This information alone is used to classify stage. Lack of an answer is coded as unknown stage. Classification is done at the registry office. (England and Wales, Norway)

(b) This information plus the treatment information is the basis for the coding of stage. Data are classified at the registry office. (Finland)

3. The patient's hospital record is abstracted specifically to acquire information on stage (as well as other items). The determination of the stage classification is made by the abstractor and checked by a reviewer at the registry office.

(a) Abstracted and classified by a doctor. (Denmark, certain sites; France)

(b) Abstracted and classified usually by a lay clerk. Specific provision is made for an unknown stage category. (USA)

Even without any evaluation of the reliability of the various systems, it is obvious that such differences in the mechanics of data collection and classification offer no assurance of obtaining comparable results.

Furthermore, even with the same general system, widely different results can be obtained. For example, the British and Norwegian systems are essentially the same. However, there is not a single case classified as "unknown stage" in the British data for colon and rectum. In general, this category is rarely used for any cancer site. On the other hand, the Norwegian percentage of unstaged cases is among the highest for colon and rectum, and the category is rarely unused for any site. It is conceivable that the question on the reporting form is phrased in such a way that while there is some chance that a Norwegian doctor might not reply, a British doctor would always answer. This argument is not convincing. There must be some additional differences in the ground rules—possibly in editing or coding procedures.

Here again, there may be a reflection of the "death certificate only" reporting problem. As indicated earlier, these cases are more often included in the Norwegian data than in data from elsewhere. The British collection system is such that I think "death certificate only" cases would never be registered. A part of the difference in the percentage unstaged could be ascribed to the differential coverage of "death certificate only" cases since they could normally be properly classified as "unknown stage at diagnosis or treatment." Without further information, it is impossible to assess the relative importance of this partial explanation as opposed to the influence of basic differences in methods of collecting and coding specific data on stage of disease.

In particular, one notes that the American data are also high in the proportion of "unstaged" cases. The outline above suggests that the fact

that there is specific provision on the American report form for a stage unknown category may be important. On the abstract forms of the other registries there is no such indication that unknown stage might be an acceptable entry.

Before further large studies are undertaken, it is suggested that intensive investigation of staging systems and criteria be attempted. As a start, each registry might initiate a review of its unstaged cases.

#### D. Too Few Age Groups in the Tabulations

Next, your attention is directed to the possible influence of the age grouping of the tabulated data. The specific age groups for each site were agreed upon at the meeting in Copenhagen in October of 1959. For some sites, cervix uteri, for example, relatively detailed age groupings were decided upon. For most sites a small, and to my mind inadequate, number of age groups was adopted.<sup>4</sup>

There are two general situations wherein an inadequate number of age groups might bias the comparison of end results. The first and more important concerns the condition in which age or physiological factors associated with age govern the choice of treatment. The second is the differential age structure of the populations of the countries here represented.

As an example, older patients may not receive surgery even in a country where surgery would otherwise be the treatment of choice. Since one of the purposes of this Group is to assess the relative merits of various types of therapy, it becomes important to be able to separate this additional complication in the selection of treatment method. Small age groups, each studied independently, would permit an appropriate analysis.

Second, the general populations of the countries here represented by their cancer cases differ in age composition. France, England, and Norway have older populations than Finland; the United States and Denmark are intermediate. Comparative studies based only on large age groups can be misleading, especially if the older age-groups are too broad.

For both reasons, therefore, I urge that in future studies tabulations be provided containing detailed age grouping of the data, such as at 10-year intervals. Let the analyst combine the data as needed.

#### E. Summary

In concluding Section I, I wish to stress that although the points I have discussed highlight some of the difficulties inherent in our collaborative studies, they should not be a cause for pessimism. In fact, such examination of possible lack of comparability also helps to explain some of the

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<sup>4</sup> It should be realized that at that time it was not foreseen that most of the tabulations would be derived from common use of a computer. The original plan was for each registry to provide its own tabulations. The age groups were restricted, in part, to reduce the volume of work for registries not having easy access to an electronic computer.

differences in the data and to make us cautious in our interpretations. As guidance for future studies emphasis is given to intensive investigation of all definitions and procedural methods. Also accentuated is the need to acquire all the data, not just a segment, no matter how well defined the segment may be. Furthermore, the analyst should be provided with detailed tabulations and not handicapped by previous decisions.

## II. PROBLEMS OF CONVERSION TO ONE SPECIFIC CODING SYSTEM

### A. Introduction

In the previous Section of this Appendix were considered the peculiar comparability problems wherein the data *not* examined were the source of difficulty. In this Section will be discussed the more usual problems of differing classifications of the data that are to be examined.

The U.S. representatives to this Group had offered to prepare for other countries tabulations of their own data similar to those we were preparing for this conference from the U.S. data. Unfortunately, because of limitations of time, budget, and computer availability, we were limited precisely to the format and programming rules planned for those tabulations and could not deviate. Therefore, we had to insist that we be supplied with punch cards which were coded in a manner compatible with our own system.<sup>5</sup> The other registries devoted much effort to satisfying this requirement. Certainly the provision of tabulations has been a cooperative venture. However, because of the need to force various definitional systems into one common classification system, the uniformly presented tables may conceal basic differences. The following remarks explore some of the important areas where possible misconceptions in interpreting the data can be avoided by examining the conversion problems and the attempts to remove discrepancies when possible.

It should be emphasized that, because of the anticipated conversion to the U.S. punch card code, advance efforts were made to solve problems expected from known differences in definition or classification. During a relatively short period much time, energy, and expense were devoted to reviewing records, obtaining additional information, and recoding. It is fair to state that intensive action was undertaken to achieve complete comparability or to approximate it closely. However, the differences between certain coding schemes on some specific items were too basic to be overcome

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<sup>5</sup> Incidentally, just because we were forced to base the tabulations upon the U.S. coding system does not mean that the American analysts are happy with all the details and definitions of that system. On the contrary, the Uniform Punch Card code is in process of change. The fact that it was used rather than the code of one of the other registries was purely a matter of expediency. However, since it is a relatively crude code, it was probably easier to condense the other classification systems to fit the UPC code than to convert the American data to a more detailed system.



in the short time before tabulations were required. In fact, some of the differences came to light only after the tabulations were completed.

### B. Survival Time

In regard to survival time, the basic datum of the analysis, the question concerned how it was computed at the various registries or essentially how were the dates defined that served as endpoints. Let us first consider the starting point.

As recommended by Dr. McKenzie, survival was to be measured from the date of first treatment except for the untreated<sup>6</sup> case whose survival should be computed from date of diagnosis. There is no disagreement concerning the completely untreated case. However, for the treated case the U.S. data is supposed to be based on date of diagnosis rather than treatment, whereas the other countries have definitions using date of first treatment as a starting point. Realistically and operationally the definitions are rarely followed precisely. The common basic date in almost all records, regardless of definition, is the date of admission to the hospital. There is, therefore, no important problem in comparability here. Even for cancers which are rapidly fatal and where a small time difference might be important, such a difference would be noticeable only if survival were measured in months or weeks rather than in years as in the present analysis.

In regard to the endpoint, there is no difficulty concerning patients known to have died; the date of death, of course, is always used. However, for the patient alive at last contact there were differences in method of obtaining follow-up information and in definition of the date to which the patient had survived.

The American follow-up procedure is that registry personnel attempt to follow a previous patient at least once a year until death. French policy is to follow yearly for 10 years; then the study is over. The policy in England and Wales is to obtain follow-up information at specified anniversaries: 1, 2, 3, 4, 5, 7, 10, and 15. In contrast, the registries in Denmark, Finland, and Norway, because of close liaison with excellent death-registration systems, usually consider a patient alive for whom no death certificate has been filed. In other words, in England, France, and the United States a patient was given credit only for known survival; in Scandinavian practice there was a slight possibility that some patients might have more survival ascribed to them than was actually true.

Therefore, intensive checking procedures were undertaken in Denmark, Finland, and Norway. All cases not certified as dead were checked with the respective People's registries. (In addition, a representative of the Danish registry personally checked on all long-term survivors from stomach cancer.) It is my understanding that in Finland and

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<sup>6</sup> See the discussion of the definition of the "untreated" case in Part C of this Section.



Norway the survival-checking procedures undertaken as a special project for the Ad Hoc Group studies have become normal registry practice. At any rate, in these data it is now possible to compare with confidence the survival times as computed by the various registries.

### C. Treatment

Treatment from all the European registries (and also from Connecticut) included a classification of palliative versus radical or curative therapy. Surgery and radiation were categorized in great detail on this characteristic. Unfortunately, the concept of definitive treatment upon which the Uniform Punch Card code is based makes no distinction between radical and palliative treatment except to exclude certain types of nondefinitive palliative treatment. The definition roughly includes all cancer treatment except that which is entirely symptomatic or supportive. Therefore, all appropriate subcategories were combined to produce a code for the common punch card. This was not too difficult. However, for the years of data being studied, the British surgery code was not as specific as in more recent years. There are included an unknown but probably small proportion of palliative operations which would not be classified as definitive. This inconsistency would probably affect only comparisons involving cases in the late stages of disease or the totals of all cases. In such comparisons the British data for surgically treated cases might be expected to show lower survival rates. Data from all registries appear to be comparable within the treatment categories for localized or early cases.

It was mentioned earlier that there were no essential differences in the starting date from which was computed the survival for an untreated case. However, there was and there remains in the tabulations some difference in what is operationally called an "untreated" case. On the American punch cards a patient is coded as "untreated" if he received no definitive treatment within the first 4 months after diagnosis. If, for example, treatment were initiated in the 7th month the patient would be classified as untreated in the "first course of treatment" and as treated in "subsequent treatment." Only the "first course of treatment" was considered for these cooperative studies. Therefore, in addition to those patients who were never definitively treated, there are also some patients coded as untreated who actually were treated more than 4 months after diagnosis. Since the European registries, in general, would compute survival time from the date of treatment and would classify such cases as treated, there is obviously a lack of comparability here. The number of discrepant American cases is probably small and very likely in the nonlocalized category. However, it is possible that leukemia comparisons might be affected. So-called "subsequent treatment" by chemotherapeutic agents would very likely extend the lifespan of the child with leukemia who is coded as "untreated" in the "first course of therapy."

#### D. Stage of Disease

"Stage" is a difficult concept and is still one of the frontiers in classification. For many sites there are no standard or accepted staging schemes. For some sites there are competing classifications for stage. There are clinical staging systems which ignore histological evidence, and there are schemes which contain consideration of such laboratory results.

Further complications result from differences among the medical specialists. Surgeons can review their preoperative staging assessments by having the pathologists examine a variable portion of the surgical specimen. Radiologists, however, must usually stand by their pretreatment classification; they are not favored with such an opportunity for a second guess. There may be an innate difference between staging as done by the surgeons and by the radiologists.

Accepting all of these hazards, the Ad Hoc Group agreed to rough definitions of "localized" and "nonlocalized" spread. It was agreed that *in situ* cases would be omitted and certain registries reviewed coding to be certain that such cases could be separately identified.

A more difficult problem, especially for one registry, was the review of cases to ensure that patients with "direct extension to neighboring organs" were no longer classified as localized. This type of case is a problem in classification to many registries and, unfortunately, few can identify this subgroup separately. There is agreement, apparently, that direct extension with *invasion* of neighboring organs is not to be considered "localized" spread. I am not certain of the uniformity of the policy or of the practice in classifying direct extension *to* or *adhering to* other organs *without mention of invasion*. It is possible but doubtful that this usually minor point might contribute to an explanation of the differences between countries in survival rates for localized cancers.

Before these collaborative studies were begun, not all the countries here represented collected or routinely classified data on stage of disease. Of course, it was no surprise to discover that the French, who pioneered much of the work on staging, had detailed and precise information on both their abstract form and their punch card. The Norwegian cancer registry collected and routinely coded stage of disease for breast and cervix cases, but not for other cancers. The British also coded information on breast and cervix cases in accordance with the internationally proposed classifications, but in addition classified other cancers as "early" (localized) or "late" (nonlocalized). The Danish cancer registry collected information on stage of disease for cases hospitalized as of January 1960 and later. Therefore, much effort was expended to acquire staging information retrospectively for patients of earlier years with certain specified cancers.

The Danish cancer registry staff obtained stage information from the hospitals specifically for cervix uteri, corpus uteri, rectum, and sigmoid colon cases. For stomach cancers the staging was based on whether the

reports to the registry had specified the initial treatment as radical or palliative. Radical treatment was coded as localized stage and palliative treatment was coded as nonlocalized stage.

In a somewhat similar fashion the Finnish cancer registry used the fact of radical or palliative treatment *in conjunction with* information on the abstract form concerning the presence and location of metastases to establish a compatible stage code for all cancers.

On the Norwegian report form there was a question whether the presence of metastases had been demonstrated. Replies to this question became the basis of approximating the stage classification code of the Uniform Punch Card. It is possible that if treatment information had also been considered, a more precise approximation of stage would have been achieved.

As mentioned earlier, the Danish data for the staging of sigmoid colon were very precise. However, the Ad Hoc Group did not decide to study sigmoid colon, but the entire large intestine. The Danish stage-of-disease data pertaining to the remaining parts of the colon were not as definitively coded as for the sigmoid. Therefore, only totals for the colon were presented for the Danish data to avoid misinterpretation of distribution or survival figures for specific stage categories.

#### E. Primary Site

Most of the sites selected for study were relatively easy to identify at each of the respective registries. Almost all used the WHO's International Statistical Classification of Diseases, Injuries, and Causes of Death. (The Danish registry had a detailed classification of diagnoses which was readily convertible into the ISC code.) However, usage of the same numbers does not always assure complete agreement of content. For example, it was discovered that the U.S. and Norwegian registries interpreted the code numbers for colon and rectum differently.<sup>7</sup> The U.S. data had rectosigmoid cancers coded as rectal cancers; the Norwegian data had rectosigmoid cancers coded as cancers of the sigmoid colon. Because few other anatomical sites are subdivided into competing code numbers, it is unlikely that there are similar differences in the interpretation of other ISC codes. However, this one example points out how detailed must be the investigation into definitions to assure complete comparability.

#### F. Final Summary

Despite the long discussion concerning possible differences in comparability, how severe an impact the differences may have created in the final figures is unknown. It is true that if the work were to be repeated, we could now do a somewhat better job. No harm is caused by emphasis on

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<sup>7</sup> See paper by Eisenberg, Mork, and Connelly in these proceedings.



the need for caution in the interpretation. However, if one reviews in detail all of the points made in this discussion, it becomes evident that rarely is the localized case affected. Therefore, it is this author's belief that, except for the possible age-group bias, *the data and calculations for localized cancers are essentially comparable*. I cannot make the same statement for the nonlocalized cancers nor for the totals of all cancers of particular sites. Since the evaluation of end results is especially meaningful for those patients for whom cure is thought possible and to whom treatment is given with the intent of cure, and since localized cancers are usually in this category, the primary purpose of the Ad Hoc Group study has been achieved—the production of end results data which can usefully be compared.



## Computation of Survival Rates

### OBSERVED RATES

**S**URVIVAL rates for each defined group of patients were computed by the actuarial, or life-table, method. These rates were based on information available on each patient, namely, date of diagnosis (or initiation of treatment), date of last contact or death, vital status at last contact (alive or dead), and survival time. The computations were performed by recording for each 1-year interval of follow-up:

- (a) the number alive at the beginning of the interval,
- (b) the number died during the interval, and
- (c) the number withdrawn alive or lost to follow-up during the interval.

To illustrate the method let us consider a hypothetical group of 1,000 patients diagnosed during the 10-year interval 1946-55; 100 patients were diagnosed in each year; patients were followed through December 31, 1960. All patients were under observation for at least 5 years, but only those patients diagnosed from 1946 to 1950 were observed for a full 10 years. Although patients diagnosed during calendar years 1951 through 1955 were under observation for less than 10 years, useful information for part of the 10-year interval is available on these patients. The life-table method utilizes all available information. The computations are summarized in table A; the columns of this table are explained below:

- Col. 1. Year of observation ( $x$  to  $x + 1$ ). Time elapsed from date of diagnosis in intervals of 1 year.
- Col. 2. Alive at beginning of interval ( $l_x$ ). The first entry in this column is the number of patients at diagnosis, which should equal the sum of the entries in columns 3, 4, and 5. Successive entries in this column are obtained according to the formula:
$$l_{x+1} = l_x - (d_x + u_x + w_x).$$
- Col. 3. Died during interval ( $d_x$ ).
- Col. 4. Lost to follow-up during interval ( $u_x$ ). Number of patients whose survival status as of December 31, 1960, was unknown. The length of observation for each patient is the time elapsed from date of diagnosis to date of last contact.

TABLE A.—Computation of survival rates for 10 years (patients treated 1946–1955 and followed through December 31, 1960)

Year of observation (1) $x$ to $x+1$	Alive at beginning of interval (2) $l_x$	Died during interval (3) $d_x$	Lost to follow-up during interval (4) $u_x$	Withdrawn alive during interval (5) $w_x$	Effective number exposed to the risk of dying (Col. 2— $\frac{1}{2}$ Col. 4— $\frac{1}{2}$ Col. 5) (6) $l'_x$	Proportion dying (Col. 3 ÷ Col. 6) (7) $q_x$	Proportion surviving (1—Col. 7) (8) $p_x$	Cumulative proportion surviving ( $p_1 \times p_2 \times \dots \times p_x$ ) (9) $P_x$
0–1	1000	180	4		998	.180	.820	.820
1–2	816	170	4		814	.209	.791	.649
2–3	642	80	4		640	.125	.875	.568
3–4	558	50	4		556	.090	.910	.517
4–5	504	40	4		502	.080	.920	.476
5–6	460	28	6	44	435	.064	.936	.446
6–7	382	26	5	43	358	.073	.927	.413
7–8	308	7	4	38	287	.024	.976	.403
8–9	259	7	3	37	239	.029	.971	.391
9–10	212	11	3	33	194	.057	.943	.369
10–11	165		3	165				

- Col. 5. Withdrawn alive during interval ( $w_x$ ). Number of patients known to have been alive on December 31, 1960. The length of observation for each patient is the time elapsed from date of diagnosis to December 31, 1960.
- Col. 6. Effective number exposed to risk of dying ( $l'_x$ ). It is assumed that patients lost or withdrawn from observation during an interval were exposed to the risk of dying, on the average, for one half of the interval. The effective number exposed is obtained by the formula:

$$l'_x = l_x - \frac{1}{2} (u_x + w_x).$$

- Col. 7. Proportion dying during the interval ( $q_x$ ).

$$q_x = d_x \div l'_x.$$

- Col. 8. Proportion surviving the interval ( $p_x$ ).

$$p_x = 1 - q_x.$$

- Col. 9. Cumulative proportion surviving ( $P_x$ ). This is generally referred to as the cumulative survival rate, and is obtained by cumulatively multiplying the proportion surviving each interval:

$$P_x = p_1 \times p_2 \times p_3 \dots p_x.$$

The successive entries in this column give the 1-year, 2-year, . . . . . and 10-year cumulative survival rates.

The above computing procedure is based on the assumption that, for cases withdrawn alive and cases lost to follow-up, survival subsequent to date of last contact is similar to that for cases with complete follow-up information. This assumption is probably more valid for cases withdrawn from observation than for cases lost to follow-up. As a rule of thumb, survival rates based on a series in which more than 10 percent of the cases were lost should be used with extreme caution.

The actuarial method of computation utilizes all survival information accumulated up to the closing date of the study. The advantages of the method were described in detail by Cutler and Ederer (1).

## CORRECTED OR RELATIVE RATES

The observed survival rate reflects mortality not only from the disease under study, but also deaths from all other causes. Since accurate information on cause of death is generally not available for large series of patients, adjustment for deaths from causes other than the specific disease under study must be made by an indirect method. The corrected or relative survival rate provides such an adjustment. It is defined as the ratio of the observed survival rate to the expected rate for a group of people in the general population similar to the patient group with respect to race, sex, age, geographic area, and calendar period of observation.

Thus, meaningful comparisons may be made among patient groups which differ with respect to "normal" mortality risk, because they were drawn from populations that differ with respect to specified demographic characteristics.

Expected survival rates (or probabilities) were estimated through the use of general population life tables for each country. The procedure was as follows:

1. The survival probability for each individual patient was obtained for each annual interval of follow-up, taking into account his age at the beginning of the interval.
2. The survival probability for each patient over a series of intervals is equal to the products of the annual probabilities.
3. The survival probability for a group of patients is obtained by summing the individual probabilities and dividing by the number of patients.

The above procedure, which has been referred to as *an exact method*, was feasible because of the availability of a large computer. An approximate method for computing expected survival rates has been described by Ederer, Axtell, and Cutler (2).

To illustrate the effect of adjusting for "normal" mortality let us consider two patient groups that differed with respect to only one relevant demographic characteristic—age. The two groups are white male patients with cancer of the prostate and cancer of the testis diagnosed in the United States during the period 1950–54. The age distributions and the observed, expected, and relative 5-year survival rates for these two groups are given in the following table:

	<i>Prostate</i>	<i>Testis</i>
Percentage distribution by age:		
Under 45	0	75
45–54	3	11
55–64	17	5
65–74	40	6
75 and over	40	3
Total	100	100
5-Year survival rates (%):		
Observed	27	49
Expected	67	95
Relative	40	51

By adjusting for "normal" mortality, the difference between the 5-year survival rates for cancers originating in these two sites was reduced from 22 percentage points (49 to 27) to 11 percentage points (51 to 40). The latter is a more meaningful measure of the difference in mortality associated with cancers of the prostate and the testis.

The foregoing example was selected because of the striking difference in the age distributions of the two patient groups. In considering the data presented at this Symposium we are primarily concerned with comparison



of survival rates in different countries among patients with a specified form of cancer. It is well to note that the relative survival rate adjusts for *normal mortality* only. It does not adjust for differences in deaths due to cancer, which may be associated with the age of patients. For example, surgery may be the universal treatment of choice for a specified cancer, but is less likely to be used in treating elderly patients. Thus, the computed relative survival rate for a country may be low, because a large proportion of patients are elderly. It is possible to take care of this problem by examining the relative survival rates for specific age groups. As pointed out by Lourie in his discussion of the comparability of data, an inadequate number of age groups was used for several sites.

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## Survival Tables

THE tables that follow provide a uniformly organized set of data for the various forms of cancer reported on at this Symposium. One-year and 5-year relative survival rates are given by sex for each method of treatment and for the total of treated and untreated patients. Separate figures are given for all cases reported as cancer (Confirmed and Not Confirmed—combined) and for cases with microscopically confirmed diagnoses (Confirmed only). Separate figures are given for the combination of patients with Localized and Not Localized tumors (all stages) and for patients with tumors classified as Localized.

The number of patients in each subgroup is shown to give the reader a basis for assessing the statistical reliability of the computed rate. The survival rate is not shown if there were less than 25 patients in a subgroup.

To conserve space these tables are restricted to all ages combined. Some of the papers in the body of this report include data for specific age groups. However, tabulated data by age are available for all cancers reported on at this Symposium as follows:

<i>Site</i>	<i>Age groups</i>
Tongue	0-64; 65+
Esophagus	0-69; 70+
Stomach	0-59; 60+
Large intestine	0-64; 65+
Rectum	0-64; 65+
Lung and bronchus	0-54; 55+
Female breast	0-44; 45-54; 55-64; 65+
Uterine cervix	0-34; 35-44; 45-54; 55-64; 65+
Uterine corpus	0-34; 35-44; 45-54; 55-64; 65+
Ovary	0-44; 45-59; 60+
Prostate	0-69; 70+
Testis	0-34; 35-44; 45+
Melanoma	0-9; 10-19; 20-39; 40-59; 60+
Leukemia—total	0-9; 10-19; 20-39; 40-59; 60+
Acute leukemias	0-9; 10-19; 20-39; 40-59; 60+
Chronic leukemias	0-9; 10-19; 20-39; 40-59; 60+

The editor will attempt to honor requests for supplementary data on specified groups of patients.

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*One- and five-year relative survival rates by stage of disease, confirmation of diagnosis, and method of treatment. (Relative survival rates are obtained by adjusting observed rates for normal life expectancy in each country.)*

Registry and period of diagnosis	Total, treated and untreated cases		Surgery		Radiation		Surgery and radiation		Chemohormones only		No known first course of therapy			
	Total num-ber of cases	Relative sur-vival rates 1 year 5 years	Total num-ber of cases	Relative sur-vival rates 1 year 5 years	Total num-ber of cases	Relative sur-vival rates 1 year 5 years	Total num-ber of cases	Relative sur-vival rates 1 year 5 years	Total num-ber of cases	Relative sur-vival rates 1 year 5 years	Total num-ber of cases	Relative sur-vival rates 1 year 5 years		
Tongue (International List No. 141)—Male														
<i>1945-49</i> ALL STAGES  <i>Confirmed and Not Confirmed</i>	Connecticut	131	0.56	0.23	42	0.76	0.47	64	0.49	0.16	15	10		
	England and Wales <sup>1</sup>	974	.51	.27	43	.72	.56	648	.51	.26	168	114	0.09	0.01
	U.S. Central	411	.56	.26	101	.79	.56	219	.51	.19	32	54	.31	.06
	U.S. Hospital	225	.60	.27	22			171	.57	.25	24	8		
	<i>Confirmed only</i>													
	Connecticut	120	.59	.25	42	.76	.47	59	.51	.18	12	7		
	England and Wales <sup>1</sup>	523	.61	.33	39	.77	.58	327	.56	.29	142	14		
	U.S. Central	364	.59	.28	99	.79	.54	196	.55	.20	29	35	.33	.00
	U.S. Hospital	218	.60	.27	22			165	.58	.26	24	7		
	LOCALIZED													
<i>Confirmed and Not Confirmed</i>	Connecticut	61	.70	.39	28	.88	.63	26	.60	.24	3	4		
	England and Wales <sup>1</sup>	321	.80	.55	32	.90	.72	204	.78	.54	81	4		
	U.S. Central	158	.75	.49	65	.88	.74	71	.71	.37	6	15		
	U.S. Hospital	74	.87	.57	13			51	.88	.54	8	2		
	<i>Confirmed only</i>													
	Connecticut	57	.71	.42	28	.88	.63	24			2	3		
	England and Wales <sup>1</sup>	227	.81	.56	30	.93	.72	131	.78	.55	65	1		
	U.S. Central	147	.77	.51	63	.87	.72	67	.73	.39	5	11		
	U.S. Hospital	74	.87	.57	13			51	.88	.54	8	2		



1960-64 ALL STAGES											
Confirmed and Not Confirmed											
Connecticut	165	.62	.30	54	.79	.52	82	.57	.17	17	12
England and Wales <sup>1</sup>	901	.56	.31	50	.77	.46	645	.58	.30	117	84
Finland <sup>2</sup>	52	.64	.39	4			23			18	7
France <sup>3</sup>	4,155	.51	.21								
Norway <sup>3</sup>	59	.61	.30	1			44	.56	.21	13	1
U.S. Central	534	.60	.31	133	.81	.51	301	.55	.26	41	59
U.S. Hospital	265	.61	.25	45	.78	.45	172	.58	.23	17	31
Confirmed only											
Connecticut	154	.64	.29	53	.78	.51	76	.59	.14	16	9
England and Wales <sup>1</sup>	525	.66	.39	40	.77	.52	359	.67	.38	103	18
Finland <sup>2</sup>	47	.67	.39	4			22			18	3
France <sup>6</sup>											
Norway <sup>1</sup>	55	.64	.31	1			41	.58	.23	13	
U.S. Central	507	.61	.31	132	.81	.50	287	.56	.26	40	48
U.S. Hospital	259	.61	.25	43	.77	.44	171	.58	.24	17	28
Localized											
Confirmed and Not Confirmed											
Connecticut	84	.82	.49	37	.85	.64	39	.84	.28	7	1
England and Wales <sup>1</sup>	327	.81	.54	29	.93	.61	240	.80	.51	49	7
Finland <sup>2</sup>	35	.75	.57	4			16			12	3
France <sup>3</sup>	1,425	.70	.40								
Norway <sup>3</sup>	31	.70	.41	1			21			9	
U.S. Central	220	.80	.52	79	.91	.69	115	.76	.46	12	14
U.S. Hospital	103	.79	.47	20			64	.77	.43	6	13
Confirmed only											
Connecticut	82	.83	.49	37	.85	.64	37	.85	.26	7	1
England and Wales <sup>1</sup>	230	.87	.59	23			164	.87	.56	41	
Finland <sup>2</sup>	33	.73	.57	4			16			12	1
France <sup>6</sup>											
Norway <sup>1</sup>	30	.72	.42	1			20			9	
U.S. Central	213	.81	.52	79	.91	.69	111	.76	.45	12	11
U.S. Hospital	101	.78	.46	18			64	.77	.43	6	13

See footnotes at end of Appendix table.

*One- and five-year relative survival rates by stage of disease, confirmation of diagnosis, and method of treatment. (Relative survival rates are obtained by adjusting observed rates for normal life expectancy in each country)—Continued*

Registry and period of diagnosis	Total, treated and untreated cases		Surgery		Radiation		Surgery and radiation		Chemo/hormones only		No known first course of therapy	
	Total num-ber of cases	Relative sur-vival rates 1 year 5 years	Total num-ber of cases	Relative sur-vival rates 1 year 5 years	Total num-ber of cases	Relative sur-vival rates 1 year 5 years	Total num-ber of cases	Relative sur-vival rates 1 year 5 years	Total num-ber of cases	Relative sur-vival rates 1 year 5 years	Total num-ber of cases	Relative sur-vival rates 1 year 5 years
Tongue (International List No. 141)—Female												
<i>1945-49</i> ALL STAGES  <i>Confirmed and Not Confirmed</i> Connecticut England and Wales 1 U.S. Central U.S. Hospital <i>Confirmed only</i> Connecticut England and Wales 1 U.S. Central U.S. Hospital	36	0.66	0.48	18	10	0.60	0.41	4	0.70	0.32	4	4
	327	.61	.39	19	213	.60	.41	72	.70	.32	72	23
	108	.72	.42	34	42	.60	.30	15			15	17
	59	.80	.39	6	38	.73	.20	12			12	3
	30	.66	.41	15	10			4			4	1
	208	.67	.44	16	125	.65	.47	64	.72	.32	64	3
	96	.73	.42	31	39	.62	.32	15			15	11
	57	.81	.40	6	37	.75	.20	12			12	2
	25	.83	.63	16	5			2			2	2
	156	.82	.58	11	100	.83	.60	41	.75	.43	41	4
<i>Confirmed and Not Confirmed</i> Connecticut England and Wales 1 U.S. Central U.S. Hospital <i>Confirmed only</i> Connecticut England and Wales 1 U.S. Central U.S. Hospital	61	.88	.62	28	17	.99	.77	7			7	9
	26	.91	.71	5	12			7			7	2
	20			13	5			2			2	
	120	.82	.59	9	75	.81	.62	35	.79	.43	35	1
	56	.89	.59	25	17	.99	.72	7			7	7
	26	.91	.71	5	12			7			7	2

1950-54 ALL STAGES														
Confirmed and Not Confirmed														
Connecticut	45	.73	.46	22	.83	.67	14	.65	.43	6	.75	.38	2	3
England and Wales 2	346	.65	.42	27			234			63				20
Finland 3	48	.69	.42	5			20			21				2
France 4 5	580	.66	.37											
Norway 3	55	.63	.45	1			27	.43	.19	24				3
U.S. Central	133	.69	.45	57	.78	.56	49	.65	.39	14				13
U.S. Hospital	57	.63	.44	16			33	.66	.43	5				3
Confirmed only														
Connecticut	44	.75	.47	21			14			6				3
England and Wales 2	239	.74	.46	24			153	.73	.49	58	.77	.35	1	3
Finland 3	45	.71	.45	5			18			21				1
France 6														
Norway 3	50	.69	.49	1			25	.46	.20	24				
U.S. Central	130	.70	.46	56	.79	.57	48	.67	.40	14				12
U.S. Hospital	57	.63	.44	16			33	.66	.43	5				3
LOCALIZED														
Confirmed and Not Confirmed														
Connecticut	25	.95	.61	14			6			4				1
England and Wales 2	179	.88	.57	24			118	.89	.61	34	.88	.39	1	2
Finland 3	35	.77	.52	5			15			15				
France 4 5	255	.80	.53											
Norway 3	46	.73	.51	1			21			23				1
U.S. Central	71	.86	.60	37	.90	.68	24			7				3
U.S. Hospital	32	.83	.64	14			17			1				
Confirmed only														
Connecticut	25	.95	.61	14			6			4				1
England and Wales 2	146	.88	.57	21			93	.90	.63	30	.89	.31	1	1
Finland 3	34	.76	.53	5			14			15				
France 6														
Norway 3	45	.74	.51	1			21			23				3
U.S. Central	70	.87	.61	37	.90	.68	23			7				
U.S. Hospital	32	.83	.64	14			17			1				

See footnotes at end of Appendix table.





1950-54		ALL STAGES																			
Confirmed and Not Confirmed																					
Confirmed and Not Confirmed	Connecticut	344	.15	.03	76	.32	.08	86	.17	.03	21	.18	.00	57	0.10	0.00	161	.06	.00		
	England and Wales 2	941	.13	.04	279	.21	.08	234	.13	.02	30						341	.05	.01		
	Finland 3	517	.18	.02	9			129	.30	.04	6						373	.13	.01		
	France 4 5	4,380	.19	.02																	
	Norway 3	280	.17	.01	24			168	.17	.01	5						83	.08	.02		
	U.S. Central	763	.17	.03	201	.34	.09	185	.15	.01	29	.21	.00	1			348	.07	.00		
	U.S. Hospital	273	.22	.01	100	.33	.02	54	.17	.02	13						105	.12	.00		
	Confirmed only																				
	Connecticut	280	.17	.03	69	.33	.09	75	.18	.03	19						117	.06	.00		
	England and Wales 2	633	.15	.04	228	.24	.08	152	.12	.02	23						187	.07	.02		
LOCALIZED	Finland 3	214	.27	.03	9			95	.35	.03	5						105	.19	.01		
	France 4 5	2,164	.20	.02																	
	Norway 3	203	.19	.01	23			143	.19	.01	5						32	.03	.00		
	U.S. Central	644	.18	.03	193	.35	.10	159	.17	.02	26	.24	.00	1			266	.07	.00		
	U.S. Hospital	238	.24	.02	98	.34	.03	49	.19	.03	13						77	.12	.00		
	Confirmed and Not confirmed																				
	Connecticut	112	.15	.03	28	.30	.08	30	.14	.04	8						46	.05	.00		
	England and Wales 2	176	.28	.10	89	.35	.13	41	.23	.07	5			6			35	.11	.05		
	Finland 3	295	.21	.03	7			96	.30	.04	3						189	.15	.00		
	France 4 5	182	.29	.02																	
Confirmed only	Norway 3	169	.18	.01	7			121	.20	.01	1						40	.14	.04		
	U.S. Central	209	.21	.05	58	.41	.14	62	.17	.02	8						81	.09	.00		
	U.S. Hospital	59	.26	.05	22			13			4						20				
	Confirmed only																				
	Connecticut	90	.19	.04	25	.33	.09	26	.16	.05	6			1			33	.06	.00		
	England and Wales 2	129	.32	.10	81	.37	.13	25	.25	.05	3						19				
	Finland 3	129	.31	.04	7			70	.34	.02	3						49	.23	.02		
	France 4 5	104	.31	.02																	
	Norway 3	116	.21	.01	7			99	.23	.01	1						9		.00		
	U.S. Central	174	.24	.06	54	.42	.15	56	.19	.02	6						58	.11			
U.S. Hospital	54	.27	.05	22			11			4						17					

See footnotes at end of Appendix table.

*One- and five-year relative survival rates by stage of disease, confirmation of diagnosis, and method of treatment. (Relative survival rates are obtained by adjusting observed rates for normal life expectancy in each country)—Continued*

Registry and period of diagnosis	Total, treated and untreated cases		Surgery		Radiation		Surgery and radiation		Chemotherapy hormones only		No known first course of therapy			
	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates		
		1 year		5 years		1 year		5 years		1 year		5 years	1 year	5 years
Esophagus (International List No. 150)—Female														
<i>1945-49</i> ALL STAGES  <i>Confirmed and Not Confirmed</i> Connecticut England and Wales <sup>1</sup> U.S. Central U.S. Hospital <i>Confirmed only</i> Connecticut England and Wales <sup>1</sup> U.S. Central U.S. Hospital	50	0.21	0.05	9	0.22	0.06	8	0.19	0.04	6		27	0.08	0.00
	447	.14	.03	138	.33	.18	127	.21	.03	24		157	.04	.00
	129	.16	.05	25	.33	.18	24			6		74	.09	.02
	48	.19	.07	13			6					29	.07	.00
	37	.25	.06	9	.28	.08	6	.21	.03	5		17		.00
	247	.19	.04	95	.33	.18	74			15		62	.03	.00
	102	.18	.06	25			20			5		52	.09	.03
	40	.23	.09	13			5					22		
	LOCALIZED													
	<i>Confirmed and Not Confirmed</i> Connecticut England and Wales <sup>1</sup> U.S. Central U.S. Hospital <i>Confirmed only</i> Connecticut England and Wales <sup>1</sup> U.S. Central U.S. Hospital	27	.19	.05	4	.41	.12	6	.35	.09	2		15	
87		.38	.10	47			27			4		9		
40		.18	.06	6			8			2		24		
8				2			1					5		
17				4	.43	.15	5			1		7		
58		.42	.12	38			16			3		1		
28		.26	.09	6			7			1		14		
6				2								4		

## SURVIVAL TABLES

## SURVIVAL TABLES

1950-54 ALL STAGES											
Confirmed and Not Confirmed											
Connecticut	59	.23	.11	15	.27	.12	9	.23	.07	4	31
England and Wales <sup>2</sup>	552	.18	.07	211			128	.23		23	163
Finland <sup>3</sup>	521	.18	.02	4			128	.34	.02	4	388
France <sup>4</sup>	336	.22	.03								
Norway <sup>5</sup>	98	.17	.05	6			41	.25	.03	5	46
U.S. Central	161	.21	.03	52	.38	.16	32	.16	.00	5	72
U.S. Hospital	59	.27	.08	19			13			1	26
Confirmed only											
Connecticut	49	.25	.12	15			9			4	21
England and Wales <sup>2</sup>	398	.20	.09	179	.30	.15	86	.23	.10	17	90
Finland <sup>3</sup>	187	.26	.03	4			88	.38	.03	4	91
France <sup>4</sup>	152	.21	.02								
Norway <sup>5</sup>	57	.24	.06	6			31	.23	.00	5	15
U.S. Central	136	.23	.07	52	.38	.16	27	.15	.00	5	52
U.S. Hospital	51	.31	.09	18			13			1	19
LOCALIZED											
Confirmed and Not Confirmed											
Connecticut	17			7						2	8
England and Wales <sup>2</sup>	122	.32	.12	73	.38	.18	21			3	23
Finland <sup>3</sup>	308	.22	.03	3			93	.37	.03	4	208
France <sup>4</sup>											
Norway <sup>5</sup>	68	.19	.06	2			37	.25	.03	1	28
U.S. Central	49	.38	.14	17			9			2	21
U.S. Hospital	16			6			4			1	5
Confirmed only											
Connecticut	15			7						2	6
England and Wales <sup>2</sup>	93	.37	.15	68	.41	.19	12			1	10
Finland <sup>3</sup>	131	.30	.04	3			68	.41	.04	4	56
France <sup>4</sup>											
Norway <sup>5</sup>	41	.23	.06	2			27	.23	.00	1	11
U.S. Central	42	.42	.16	17			6			2	17
U.S. Hospital	15			5			4			1	5

See footnotes at end of Appendix table.

*One- and five-year relative survival rates by stage of disease, confirmation of diagnosis, and method of treatment. (Relative survival rates are obtained by adjusting observed rates for normal life expectancy in each country)—Continued*

Registry and period of diagnosis	Total, treated and untreated cases		Surgery		Radiation		Surgery and radiation		Chemo/hormones only		No known first course of therapy	
	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates
		1 year		1 year		1 year		1 year		1 year		1 year
		5 years		5 years		5 years		5 years		5 years		5 years
Stomach (International List No. 15)—Male												
1945-49												
ALL STAGES												
<i>Confirmed and Not Confirmed</i>												
Connecticut	985	0.21	0.09	305	0.48	0.24	11		3		664	0.08
England and Wales 1	2,984	.18	.06	1,135	.38	.14	44	0.14	15	0.05	1,787	.05
U.S. Central	2,511	.23	.09	796	.51	.22	34	.18	5		1,670	.10
U.S. Hospital	471	.29	.10	225	.48	.17	7		4		230	.10
<i>Confirmed only</i>												
Connecticut	605	.26	.12	290	.47	.23	4		3		307	.06
England and Wales 1	1,208	.31	.11	783	.46	.16	17		12		395	.02
U.S. Central	1,649	.27	.11	777	.51	.22	18		5		846	.06
U.S. Hospital	351	.33	.12	219	.49	.17	4		4		121	.03
LOCALIZED												
<i>Confirmed and Not Confirmed</i>												
Connecticut	284	.37	.20	119	.68	.37	2		1		162	.14
England and Wales 1	374	.58	.24	321	.62	.26	1		3		49	.23
U.S. Central	477	.45	.26	235	.72	.44	4		1		236	.17
U.S. Hospital	56	.70	.43	45	.76	.48					11	
<i>Confirmed only</i>												
Connecticut	144	.56	.31	113	.69	.37			1		30	.11
England and Wales 1	302	.61	.25	287	.64	.26	1		3		11	.11
U.S. Central	297	.60	.35	229	.73	.44			1		67	.14
U.S. Hospital	49	.72	.46	44	.77	.49					5	



1960-64  
ALL STAGES

Confirmed and Not Confirmed

	1,026	.31	.13	414	.58	.27	11		2		16	0.07	0.00	599	.12	.02
Connecticut	3,517	.27	.12	2,046	.34	.14								1,471	.17	.08
Denmark	3,540	.21	.07	1,574	.38	.15	34	.09	.04					1,910	.06	.01
England and Wales 2	3,594	.24	.08	697	.67	.27	85	.25	.02					2,765	.12	.02
Finland 3	809	.36	.14									0.65	0.12			
France 4 5	3,454	.27	.09	1,156	.61	.23	41	.10	.00					2,240	.09	.01
Norway 3	2,402	.31	.12	982	.59	.26	28	.15	.00					1,382	.12	.02
U.S. Central	553	.27	.11	278	.43	.17	4							266	.11	.04
U.S. Hospital																
Confirmed only																
Connecticut	756	.35	.15	401	.57	.27	5							348	.09	.01
Denmark	1,633	.40	.16	1,309	.47	.19								324	.11	.02
England and Wales 2	1,789	.32	.13	1,239	.44	.18	13							525	.04	.01
Finland 3	1,321	.42	.14	631	.68	.28	25	.29	.00					618	.14	.01
France 4 5	326	.45	.19									.65	.12			
Norway 3	1,711	.44	.16	1,135	.62	.23	23							536	.07	.01
U.S. Central	1,859	.35	.14	965	.58	.25	18							867	.09	.01
U.S. Hospital	424	.31	.12	263	.45	.18	2							155	.07	.02
LOCALIZED																
Confirmed and Not Confirmed																
Connecticut	198	.54	.33	135	.71	.46	2							60	.19	.00
Denmark	1,155	.53	.23	1,155	.53	.23										
England and Wales 2	556	.51	.25	469	.57	.29	4							78	.17	.00
Finland 3	1,057	.41	.17	389	.76	.34	27	.20	.05					623	.18	.04
France 4 5	172	.62	.32													
Norway 3	961	.44	.24	414	.82	.46	8							532	.14	.01
U.S. Central	376	.58	.37	258	.76	.50	3							114	.18	.01
U.S. Hospital	57	.62	.53	44	.68	.60								13		
Confirmed only																
Connecticut	156	.62	.40	132	.70	.46								23		
Denmark	1,027	.57	.24	1,027	.57	.24										
England and Wales 2	445	.59	.30	432	.60	.30	1							10		
Finland 3	450	.67	.29	358	.76	.35	6							68	.24	.02
France 4 5	103	.70	.37													
Norway 3	455	.78	.44	406	.83	.47	3							39	.30	.11
U.S. Central	310	.65	.42	254	.76	.50	1							54	.13	.00
U.S. Hospital	51	.65	.58	43	.69	.61								8		

See footnotes at end of Appendix table.

*One- and five-year relative survival rates by stage of disease, confirmation of diagnosis, and method of treatment. (Relative survival rates are obtained by adjusting observed rates for normal life expectancy in each country)—Continued*

Registry and period of diagnosis	Total, treated and untreated cases		Surgery		Radiation		Surgery and radiation		Chemohormones only		No known first course of therapy	
	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates
		1 year		5 years		1 year		5 years		1 year		5 years
Stomach (International List No. 15)—Female												
<i>1945-49</i>												
ALL STAGES												
<i>Confirmed and Not Confirmed</i>												
Connecticut	574	.24	192	.53	6		9		1		375	.10
England and Wales <sup>1</sup>	1,739	.18	632	.36	24				3		1,071	.06
U.S. Central	1,309	.27	438	.55	17		1		6		847	.13
U.S. Hospital	179	.35	91	.56	4		1				83	.11
<i>Confirmed only</i>												
Connecticut	337	.32	187	.54	1						149	.04
England and Wales <sup>1</sup>	710	.29	454	.43	12		9		3		232	.01
U.S. Central	830	.32	431	.55	11		1		2		385	.06
U.S. Hospital	146	.37	88	.55	2		1				55	.09
LOCALIZED												
<i>Confirmed and Not Confirmed</i>												
Connecticut	153	.35	68	.64	1						84	.12
England and Wales <sup>1</sup>	214	.53	178	.58			1				35	.27
U.S. Central	256	.44	131	.69	1						124	.18
U.S. Hospital	23		20								3	
<i>Confirmed only</i>												
Connecticut	86	.54	66	.66							20	
England and Wales <sup>1</sup>	163	.60	154	.63			1				8	
U.S. Central	165	.58	128	.70							37	.14
U.S. Hospital	21		20								1	

1960-64

## ALL STAGES

*Confirmed and Not Confirmed*

	575	.29	.11	219	.53	.23	4		4	0.66	0.22	10	348	.14	.08
Connecticut	2,098	.27	.12	1,084	.37	.16							1,014	.15	.08
Denmark	2,106	.20	.07	853	.41	.15	15		2				1,226	.05	.01
England and Wales <sup>2</sup>	2,958	.21	.07	402	.64	.25	78	0.24	49				2,429	.13	.03
Finland <sup>3</sup>	463	.42	.19												
France <sup>4</sup>	2,352	.26	.10	632	.65	.28	17		22				1,681	.10	.02
Norway <sup>3</sup>	1,302	.29	.11	479	.56	.23	22		5			4	792	.13	.04
U.S. Central	222	.31	.11	111	.49	.18	1		1			1	108	.13	.03
U.S. Hospital															
<i>Confirmed only</i>															
Connecticut	390	.32	.12	215	.52	.22	2		3				179	.08	.01
Denmark	909	.39	.16	675	.49	.21							234	.07	.02
England and Wales	1,032	.31	.11	678	.46	.17	6		2			7	339	.03	.00
Finland <sup>3</sup>	877	.38	.13	366	.65	.26	29	.03	45	.63	.24		437	.15	.02
France <sup>4</sup>	171	.46	.22												
Norway <sup>3</sup>	991	.45	.18	636	.65	.28	10		22				333	.06	.00
U.S. Central	951	.32	.13	475	.55	.23	15		4			4	453	.09	.02
U.S. Hospital	180	.32	.11	109	.50	.18	1		1			1	68	.05	.00
<i>LOCALIZED</i>															
<i>Confirmed and Not Confirmed</i>															
Connecticut	103	.55	.32	64	.73	.43	1						38	.25	.11
Denmark	614	.54	.25	614	.54	.25									
England and Wales <sup>2</sup>	322	.52	.25	264	.60	.28							58	.16	.06
Finland <sup>3</sup>	878	.36	.15	218	.74	.32	22		25	.85	.40		613	.20	.07
France <sup>4</sup>	97	.60	.28												
Norway <sup>3</sup>	683	.39	.22	219	.86	.54	4		9				461	.15	.03
U.S. Central	201	.61	.33	128	.81	.49	1						72	.23	.15
U.S. Hospital	31	.53	.39	24									7		
<i>Confirmed only</i>															
Connecticut	74	.63	.36	62	.72	.43							12		
Denmark	539	.58	.26	539	.58	.26									
England and Wales <sup>2</sup>	260	.58	.27	246	.61	.29							14		
Finland <sup>3</sup>	273	.68	.30	202	.74	.33	4		23				44	.35	.14
France <sup>4</sup>	47	.66	.33												
Norway <sup>3</sup>	253	.79	.49	217	.87	.55	2		9				25	.13	.00
U.S. Central	155	.69	.43	126	.81	.49							29	.17	.11
U.S. Hospital	26	.59	.40	24									2		

See footnotes at end of Appendix table.

## SURVIVAL TABLES

*One- and five-year relative survival rates by stage of disease, confirmation of diagnosis, and method of treatment. (Relative survival rates are obtained by adjusting observed rates for normal life expectancy in each country)—Continued*

Registry and period of diagnosis	Total, treated and untreated cases		Surgery		Radiation		Surgery and radiation		Chemo/hormones only		No known first course of therapy	
	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates
		1 year		5 years		1 year		5 years		1 year		5 years
Large Intestine (International List No. 153)—Male												
1945-49 ALL STAGES												
<i>Confirmed and Not Confirmed</i>												
Connecticut	959	0.50	0.29		566	0.73	0.47		1		384	0.15
Denmark	1,273	.37	.20		876	.42	.24		17		340	.20
England and Wales <sup>1</sup>	1,703	.39	.21		1,147	.52	.30		19		518	.08
France <sup>2</sup>	73	.54	.26									.00
U.S. Central	1,901	.50	.28		1,122	.72	.45		6		738	.18
U.S. Hospital	275	.63	.38		190	.78	.51		4		76	.29
<i>Confirmed only</i>												
Connecticut	739	.63	.36		549	.74	.47		1		185	.10
Denmark	668	.50	.30		542	.53	.34		6		92	.23
England and Wales <sup>1</sup>	886	.56	.35		728	.66	.41		15	.27	137	.03
France <sup>2</sup>	35	.53	.33									
U.S. Central	1,508	.58	.34		1,103	.73	.45		4		381	.15
U.S. Hospital	229	.71	.44		186	.79	.52		1		37	.39



## SURVIVAL TABLES

LOCALIZED											
<i>Confirmed and Not Confirmed</i>											
Connecticut	378	.67	.49	.286	.82	.62	1	1	91	.13	.02
Denmark	255	.53	.38	204	.56	.52	1	10	40	.27	.15
England and Wales <sup>1</sup>	470	.76	.52	435	.79	.55	2	5	28	.31	.00
France <sup>2</sup>	31	.64	.35								
U.S. Central	656	.69	.50	505	.82	.62	1	2	146	.23	.06
U.S. Hospital	86	.89	.73	77	.93	.77			9		
<i>Confirmed only</i>											
Connecticut	317	.73	.55	277	.83	.62			40	.03	.00
Denmark	175	.61	.46	152	.62	.49		9	14		
England and Wales <sup>1</sup>	379	.81	.57	367	.82	.58	1	5	6		
France <sup>2</sup>	16										
U.S. Central	568	.75	.55	496	.83	.62		1	70	.15	.06
U.S. Hospital	82	.93	.77	76	.95	.78			6		
<i>ALL STAGES</i>											
<i>Confirmed and Not Confirmed</i>											
Connecticut	1,220	.60	.36	883	.77	.48	4	5	327	.13	.03
Denmark	1,531	.44	.26	1,146	.51	.31	12	39	334	.16	.08
England and Wales <sup>2</sup>	2,085	.48	.30	1,582	.59	.38	20	9	472	.08	.02
Finland <sup>3</sup>	334	.35	.20	70	.73	.55	19	39	205	.16	.04
France <sup>4</sup>	110	.51	.32								
Norway <sup>5</sup>	827	.45	.25	439	.74	.43	6	6	375	.10	.02
U.S. Central	2,692	.61	.38	1,901	.78	.50	8	15	635	.14	.05
U.S. Hospital	407	.65	.43	318	.77	.52	2	2	85	.19	.05
<i>Confirmed only</i>											
Connecticut	1,051	.65	.40	864	.76	.48	4	3	179	.10	.03
Denmark	1,635	.55	.34	865	.61	.37	7	31	132	.15	.07
England and Wales <sup>2</sup>	1,368	.61	.42	1,184	.69	.47	10	8	165	.06	.04
Finland <sup>3</sup>	184	.51	.31	65	.75	.55	14	36	69	.22	.07
France <sup>4</sup>	53	.57	.30								
Norway <sup>5</sup>	566	.60	.34	428	.74	.44	4	6	127	.11	.02
U.S. Central	2,365	.66	.42	1,881	.78	.50	7	13	394	.13	.05
U.S. Hospital	377	.67	.45	317	.78	.52	2	2	56	.11	.02

See footnotes at end of Appendix table.

## SURVIVAL TABLES

*One- and five-year relative survival rates by stage of disease, confirmation of diagnosis, and method of treatment. (Relative survival rates are obtained by adjusting observed rates for normal life expectancy in each country)—Continued*

Registry and period of diagnosis	Total, treated and untreated cases		Surgery		Radiation		Surgery and radiation		Chemotherapy only		No known first course of therapy	
	Total number of cases	Relative survival rates 1 year 5 years	Total number of cases	Relative survival rates 1 year 5 years	Total number of cases	Relative survival rates 1 year 5 years	Total number of cases	Relative survival rates 1 year 5 years	Total number of cases	Relative survival rates 1 year 5 years	Total number of cases	Relative survival rates 1 year 5 years
Large Intestine (International List No. 153)—Male—Continued												
1950-54 LOCALIZED												
Confirmed and Not Confirmed												
Connecticut	504	0.81	0.60	431	0.91	0.67	1	2			70	0.22 0.04
Denmark	262	.62	.43	221	.65	.47		11			30	.25 .21
England and Wales *	750	.75	.52	708	.77	.54	2	5			35	.28 .09
Finland †	110	.57	.35	44	.82	.61	4	22			40	.21 .04
France ‡	43	.87	.55									
Norway §	339	.62	.43	228	.83	.57		2			109	.15 .05
U.S. Central	982	.83	.63	847	.91	.70	1	5	1		128	.24 .12
U.S. Hospital	143	.92	.79	137	.95	.82					6	
Confirmed only												
Connecticut	472	.84	.62	425	.91	.68	1	2			44	.17 .07
Denmark	199	.70	.48	178	.71	.52		10			11	
England and Wales *	637	.79	.57	617	.80	.58	2	5			13	
Finland †	71	.74	.49	41	.85	.63	3	21			6	
France ‡	25	.81	.55									
Norway §	253	.77	.54	223	.84	.58		2			28	.14
U.S. Central	931	.85	.66	841	.91	.70	1	5	1		83	.19 .14
U.S. Hospital	143	.92	.79	137	.95	.82					6	

Large Intestine (International List No. 153)—Female

1945-49 ALL STAGES																
Confirmed and Not Confirmed																
Connecticut	1,232	0.54	0.36	774	0.77	0.55	13	0.26	0.07	7	0.59	0.17		438	0.13	0.02
Denmark	1,385	.39	.21	932	.45	.25	31			52			2	370	.22	.09
England and Wales †	1,920	.40	.23	1,284	.55	.33	25	.16	.12	18				597	.07	.02
France ‡	62	.56	.36													
U.S. Central	2,426	.55	.36	1,549	.76	.52	17			16			19	825	.17	.05
U.S. Hospital	271	.66	.46	199	.81	.59	12			6				54	.17	.08
Confirmed only																
Connecticut	954	.64	.44	751	.78	.55	9			4				190	.10	.01
Denmark	759	.52	.29	608	.57	.34	10			37	.69	.21		104	.14	.02
England and Wales †	1,098	.57	.36	901	.67	.43	15			13			1	168	.02	.00
France ‡	30	.74	.56													
U.S. Central	1,563	.63	.41	1,522	.76	.62	11			13			10	407	.13	.03
U.S. Hospital	239	.72	.50	195	.81	.59	7			6				31	.20	.07
LOCALIZED																
Confirmed and Not Confirmed																
Connecticut	513	.71	.58	395	.87	.72	2			3				113	.15	.02
Denmark	208	.57	.30	169	.56	.41				7				32	.55	.28
England and Wales †	579	.78	.52	541	.80	.55	2			6				30	.39	.15
France ‡	29	.69	.43													
U.S. Central	846	.74	.61	670	.87	.74	2			5			1	168	.22	.05
U.S. Hospital	94	.94	.85	89	.98	.89								5		
Confirmed only																
Connecticut	433	.80	.65	384	.87	.73				2				47	.15	.03
Denmark	139	.65	.45	125	.65	.48				5				9		
England and Wales†	494	.81	.55	477	.83	.57	2			4				11		
France ‡	16															
U.S. Central	738	.80	.67	657	.88	.74				4			1	76	.18	.03
U.S. Hospital	91	.96	.86	88	.98	.89								3		

See footnotes at end of Appendix table.

## SURVIVAL TABLES

*One- and five-year relative survival rates by stage of disease, confirmation of diagnosis, and method of treatment. (Relative survival rates are obtained by adjusting observed rates for normal life expectancy in each country)—Continued*

Registry and period of diagnosis	Total, treated and untreated cases		Surgery		Radiation		Surgery and radiation		Chemo/hormones only		No known first course of therapy										
	Total num-ber of cases	Relative sur-vival rates	Total num-ber of cases	Relative sur-vival rates	Total num-ber of cases	Relative sur-vival rates	Total num-ber of cases	Relative sur-vival rates	Total num-ber of cases	Relative sur-vival rates	Total num-ber of cases	Relative sur-vival rates									
		1 year		5 years		1 year		5 years		1 year		5 years	1 year	5 years							
Large Intestine (International List No. 153)—Female—Continued																					
1950-54 ALL STAGES  <i>Confirmed and Not Confirmed</i>	Connecticut	1,506	0.63	0.42	1,124	0.80	0.54	4			8		3			367	0.13	0.02			
	Denmark	1,695	.46	.29	1,257	.53	.34	16			45	0.59	0.37			377	.19	.09			
	England and Wales <sup>2</sup>	2,655	.50	.30	1,976	.63	.39	31	0.23	0.12	8		5			635	.08	.02			
	Finland <sup>3</sup>	535	.38	.21	149	.66	.46	24			58	.82	.41			304	.15	.03			
	France <sup>5</sup>	135	.49	.27																	
	Norway <sup>3</sup>	903	.44	.28	444	.75	.49	8			4			1		446	.11	.01			
	U.S. Central	3,262	.64	.43	2,462	.80	.53	13			20			20		747	.14	.05			
	U.S. Hospital	359	.66	.41	286	.77	.49	4			3			1		65	.22	.11			
	<i>Confirmed only</i>																				
	Connecticut	1,310	.69	.46	1,109	.80	.54	2			7			3			189	.10	.00		
	Denmark	1,138	.56	.37	956	.62	.41	9			36	.62	.46				137	.12	.05		
	England and Wales <sup>2</sup>	1,784	.63	.40	1,325	.72	.46	20			8			2			229	.08	.02		
	Finland <sup>3</sup>	312	.50	.29	140	.67	.45	18			55	.81	.41				99	.09	.02		
	France <sup>5</sup>	81	.54	.29																	
Norway <sup>3</sup>	571	.60	.39	435	.76	.50	4			3			1			128	.09	.00			
U.S. Central	2,933	.68	.45	2,446	.80	.53	10			19			14			444	.11	.03			
U.S. Hospital	326	.68	.44	279	.77	.50	3			3			1			40	.13	.13			



## LOCALIZED

*Confirmed and Not Confirmed*

Connecticut	594	.85	.69	536	.92	.75	1																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																																										
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## Rectum (International List No. 154)—Male

1945-49  
ALL STAGES

*Confirmed and Not Confirmed*

[illegible]

See footnotes at end of Appendix table.

*One- and five-year relative survival rates by stage of disease, confirmation of diagnosis, and method of treatment. (Relative survival rates are obtained by adjusting observed rates for normal life expectancy in each country)—Continued*

Registry and period of diagnosis	Total, treated and untreated cases		Surgery		Radiation		Surgery and radiation		Chemo/hormones only		No known first course of therapy									
	Total num-ber of cases	Relative sur-vival rates	Total num-ber of cases	Relative sur-vival rates	Total num-ber of cases	Relative sur-vival rates	Total num-ber of cases	Relative sur-vival rates	Total num-ber of cases	Relative sur-vival rates	Total num-ber of cases	Relative sur-vival rates								
		1 year		5 years		1 year		5 years		1 year		5 years	1 year	5 years	1 year	5 years				
Rectum (International List No. 154)—Male—Continued																				
1945-49 LOCALIZED  <i>Confirmed and Not Confirmed</i>	Connecticut	360	0.66	0.40	268	0.77	0.51	2	47	0.63	0.19	4	86	0.86	0.33			86	0.31	0.04
	Denmark	831	.69	.42	586	.71	.49											112	.44	.19
	England and Wales 1	886	.75	.50	798	.76	.52	13				14						61	.59	.20
	France 5	178	.57	.31																
	U.S. Central	709	.72	.46	538	.80	.55	10				7						149	.41	.11
	U.S. Hospital	140	.82	.63	105	.85	.69	14				6						15		
	<i>Confirmed only</i>																			
	Connecticut	314	.72	.45	263	.78	.51	2				4						45	.41	.07
	Denmark	667	.74	.46	506	.76	.51	34	.63	.17		73	.88	.34				54	.50	.16
	England and Wales 1	745	.78	.54	712	.79	.56	7				12						14		
	France 5	122	.59	.29																
	U.S. Central	647	.76	.49	532	.81	.55	10				7						93	.49	.16
	U.S. Hospital	138	.83	.68	105	.85	.69	13				6						14		
1950-54 ALL STAGES  <i>Confirmed and Not Confirmed</i>	Connecticut	1028	.63	.37	746	.77	.48	5				3						273	.24	.04
	Denmark	1986	.57	.26	1337	.61	.33	85	.55	.05		196	.73	.13				368	.34	.10
	England and Wales 2	2702	.56	.32	2093	.65	.39	53	.60	.13		28	.59	.08				584	.24	.03
	Finland 4	315	.49	.17	99	.71	.40	23				27	.85	.23				166	.30	.02
	France 1	418	.55	.26																

## SURVIVAL TABLES

	569	.55	.22	287	.75	.39	21		8		1	252	.29	.02
Norway <sup>3</sup>	2223	.63	.36	1537	.78	.48	19		9		17	641	.26	.06
U.S. Central	568	.66	.37	407	.77	.48	17		8			136	.32	.07
U.S. Hospital														
<i>Confirmed only</i>														
Connecticut	931	.66	.40	735	.77	.48	4		3		1	188	.25	.05
Denmark	1579	.61	.29	1133	.64	.36	66		173	.77	.13	207	.33	.08
England and Wales <sup>2</sup>	1897	.68	.42	1672	.72	.46	25		24		2	174	.26	.07
Finland <sup>3</sup>	185	.61	.23	94	.71	.43	8		26	.84	.24	57	.39	.06
France <sup>5</sup>	286	.59	.30											
Norway <sup>3</sup>	404	.65	.30	284	.75	.39	15		8		1	96	.31	.02
U.S. Central	2053	.66	.38	1526	.78	.48	18		9		14	486	.28	.07
U.S. Hospital	536	.68	.39	400	.78	.48	13		8			115	.34	.08
<i>LOCALIZED</i>														
<i>Confirmed and Not Confirmed</i>														
Connecticut	451	.82	.64	398	.88	.69	3		1			49	.39	.14
Denmark	899	.72	.41	676	.73	.46	26		74	.86	.21	123	.58	.23
England and Wales <sup>2</sup>	1100	.79	.55	1017	.80	.63	7		8		1	67	.61	.18
Finland <sup>3</sup>	138	.66	.26	68	.78	.41	9		18			43	.43	.00
France <sup>5</sup>	199	.67	.44											
Norway <sup>3</sup>	280	.64	.36	174	.81	.51	8		5			93	.30	.04
U.S. Central	897	.82	.62	754	.89	.69	7		3		2	131	.42	.17
U.S. Hospital	230	.88	.69	193	.91	.76	4		3			30	.67	.17
<i>Confirmed only</i>														
Connecticut	435	.83	.64	393	.88	.68	2		1			39	.38	.18
Denmark	776	.74	.42	621	.74	.47	20		68	.87	.20	67	.55	.14
England and Wales <sup>2</sup>	979	.81	.69	929	.82	.60	6		8		1	35	.60	.24
Finland <sup>3</sup>	103	.70	.35	66	.77	.42	4		17			16		
France <sup>5</sup>	152	.67	.46											
Norway <sup>3</sup>	212	.77	.45	173	.81	.51	6		5		2	28	.46	.07
U.S. Central	872	.82	.63	749	.88	.69	6		3			112	.44	.19
U.S. Hospital	229	.88	.69	193	.91	.76	3		3			30	.67	.17

See footnotes at end of Appendix table.





	592	80	55	459	89	62	19	13	1	100	41	22
U.S. Central U.S. Hospital	113	94	77	91	95	80	5	5		12		
<i>Confirmed only</i>												
Connecticut	240	81	56	210	87	61	4	4		22	26	22
Denmark	426	79	50	341	78	56	24	35	.96	14	.62	.22
England and Wales <sup>1</sup>	480	86	60	454	86	61	2	10				
France <sup>6</sup>	108	74	38									
U.S. Central	543	84	58	454	89	63	18	11		59	.48	.33
U.S. Hospital	112	94	77	91	95	80	4	5	1	12		
<i>1960-64</i>												
<i>ALL STAGES</i>												
<i>Confirmed and Not Confirmed</i>												
Connecticut	820	68	39	595	82	50	3	7		215	.28	.04
Denmark	1278	57	32	859	63	41	51	137	.84	231	.24	.06
England and Wales <sup>2</sup>	1865	59	34	1425	69	41	42	26	.67	371	.20	.05
Finland <sup>3</sup>	408	51	25	135	75	54	35	42	.80	196	.30	.03
France <sup>6</sup>	442	63	35									
Norway <sup>3</sup>	416	52	25	208	79	41	10	10		188	.21	.03
U.S. Central	1784	69	42	1260	84	55	22	16		480	.32	.08
U.S. Hospital	387	71	44	276	80	53	10	13		87	.47	.19
<i>Confirmed only</i>												
Connecticut	736	71	41	580	82	50	3	7		146	.27	.04
Denmark	1009	64	37	724	68	45	36	134	.85	115	.20	.07
England and Wales <sup>2</sup>	1322	71	43	1176	75	47	22	23	.21	101	.20	.08
Finland <sup>3</sup>	245	63	37	127	76	55	20	38	.83	60	.33	.06
France <sup>6</sup>	333	67	37									
Norway <sup>3</sup>	280	65	34	203	80	42	4	9		64	.20	.02
U.S. Central	1642	71	44	1244	84	55	20	16		358	.30	.09
U.S. Hospital	365	73	46	273	81	53	8	12		72	.51	.23

See footnotes at end of Appendix table.

## SURVIVAL TABLES

*One- and five-year relative survival rates by stage of disease, confirmation of diagnosis, and method of treatment. (Relative survival rates are obtained by adjusting observed rates for normal life expectancy in each country)—Continued*

Registry and period of diagnosis	Total, treated and untreated cases		Surgery		Radiation		Surgery and radiation		Chemo/hormones only		No known first course of therapy					
	Total num- num- ber of cases	Relative sur- vival rates	Total num- num- ber of cases	Relative sur- vival rates	Total num- num- ber of cases	Relative sur- vival rates	Total num- num- ber of cases	Relative sur- vival rates	Total num- num- ber of cases	Relative sur- vival rates	Total num- num- ber of cases	Relative sur- vival rates				
													1 year	5 years	1 year	5 years
Rectum (International List No. 154) Female—Continued																
1950-54 LOCALIZED																
	<i>Confirmed and Not Confirmed</i>															
	Connecticut	344	0.84	0.64	303	0.90	0.70	1				40	0.39	0.08		
	Denmark	566	.73	.51	412	.77	.61	15			64	0.92	0.33	.75	.32	.10
	England and Wales <sup>2</sup>	722	.83	.59	669	.84	.60	10			6			37	.59	.31
	Finland <sup>3</sup>	201	.69	.42	100	.82	.63	13			29	.92	.38	59	.39	.10
	France <sup>5</sup>	242	.79	.51												
	Norway <sup>3</sup>	202	.64	.37	124	.81	.49	5			8			65	.32	.07
	U.S. Central	724	.87	.69	628	.92	.75	3			3			90	.49	.22
	U.S. Hospital	165	.90	.74	138	.91	.78	3			5			19		
	<i>Confirmed only</i>															
Connecticut	328	.85	.65	299	.90	.70	1						28	.33	.06	
Denmark	480	.78	.56	366	.81	.65	12			62	.92	.32	40	.22	.11	
England and Wales <sup>2</sup>	655	.85	.61	625	.85	.61	9			5			16			
Finland <sup>3</sup>	148	.78	.51	94	.83	.64	7			27	.91	.40	20			
France <sup>5</sup>	201	.79	.49													
Norway <sup>3</sup>	155	.74	.44	122	.82	.49	2			7			24			
U.S. Central	699	.87	.70	623	.92	.75	3			3			70	.46	.25	
U.S. Hospital	163	.91	.74	137	.91	.78	3			4			19			

## SURVIVAL TABLES

Lung and Bronchus (International List No. 162.1)—Male

1945-49 ALL STAGES																			
Confirmed and Not Confirmed																			
Connecticut		786	0.16	0.03	112	0.43	0.13	197	0.12	0.01	26	0.35	0.13	9	0.04	0.00	442	0.10	0.00
England and Wales <sup>1</sup>		5942	.12	.03	419	.43	.22	2706	.14	.02	120	.31	.05	54			2643	.05	.01
U.S. Central		2135	.15	.03	267	.40	.15	403	.13	.00	36	.31	.09	15			1414	.10	.02
U.S. Hospital		637	.20	.05	123	.41	.20	171	.13	.00	29	.32	.04	9			305	.14	.02
Confirmed only																			
Connecticut		531	.17	.04	98	.45	.14	149	.12	.01	23			7			254	.08	.00
England and Wales <sup>1</sup>		2741	.14	.04	376	.46	.24	1136	.13	.01	99	.31	.05	36	.03	.00	1094	.04	.00
U.S. Central		1560	.16	.04	253	.41	.15	296	.14	.00	33	.34	.10	13			965	.09	.02
U.S. Hospital		477	.21	.06	120	.41	.20	123	.14	.00	26	.27	.00	8			200	.14	.01
LOCALIZED																			
Confirmed and Not Confirmed																			
Connecticut		258	.23	.04	45	.52	.18	55	.11	.00	6			2			150	.18	.00
England and Wales <sup>1</sup>		680	.38	.13	243	.55	.26	279	.28	.05	48	.40	.09	2			108	.25	.05
U.S. Central		419	.25	.06	94	.54	.25	82	.13	.00	8			3			232	.17	.00
U.S. Hospital		90	.45	.23	49	.60	.41	9			3			2			27	.25	.00
Confirmed only																			
Connecticut		155	.26	.06	37	.61	.22	37	.06	.00	5			2			74	.16	.00
England and Wales <sup>1</sup>		425	.42	.17	226	.56	.27	119	.22	.04	41	.40	.08	2			37	.25	.03
U.S. Central		278	.29	.09	86	.58	.27	51	.10	.00	7			3			131	.16	.00
U.S. Hospital		79	.47	.26	49	.60	.41	5			3			2			20		

See footnotes at end of Appendix table.

*One- and five-year relative survival rates by stage of disease, confirmation of diagnosis, and method of treatment. (Relative survival rates are obtained by adjusting observed rates for normal life expectancy in each country)—Continued*

Registry and period of diagnosis	Total, treated and untreated cases			Surgery			Radiation			Surgery and radiation			Chemohormones only			No known first course of therapy		
	Total number of cases	Relative survival rates		Total number of cases	Relative survival rates		Total number of cases	Relative survival rates		Total number of cases	Relative survival rates		Total number of cases	Relative survival rates		Total number of cases	Relative survival rates	
		1 year	5 years		1 year	5 years		1 year	5 years		1 year	5 years		1 year	5 years			
Lung and Bronchus (International List No. 162.1)—Male—Continued																		
1950-54 ALL STAGES  <i>Confirmed and Not Confirmed</i> Connecticut England and Wales <sup>2</sup> Finland <sup>3</sup> France <sup>4</sup> Norway <sup>3</sup> U.S. Central U.S. Hospital <i>Confirmed only</i> Connecticut England and Wales <sup>2</sup> Finland <sup>3</sup> France <sup>4</sup> Norway <sup>3</sup> U.S. Central U.S. Hospital	1451	0.19	0.04	307	0.43	0.16	329	0.12	0.00	51	0.28	0.04	20	0.12	0.01	744	0.11	0.01
	10373	.19	.05	1171	.58	.31	4849	.16	.02	199	.37	.06	110	.01	.01	4044	.09	.01
	3082	.24	.06	190	.45	.24	1117	.28	.04	136	.55	.12				1639	.16	.04
	4021	.23	.05	181	.62	.19	3116	.21	.04	196	.30	.11	4			528	.10	.04
	659	.26	.08	130	.58	.30	188	.15	.00	47	.73	.19				290	.11	.02
	3673	.20	.05	753	.48	.18	798	.15	.00	108	.30	.03	63	.07	.02	1951	.12	.01
	1318	.21	.06	301	.42	.21	304	.16	.02	58	.40	.10	96	.11	.00	559	.11	.02
	1076	.20	.05	291	.43	.16	254	.11	.00	48	.28	.05	12			471	.09	.00
	5219	.23	.08	1103	.58	.31	2061	.16	.01	178	.38	.06	56	.07	.00	1821	.08	.00
	1411	.27	.06	167	.46	.23	679	.27	.03	115	.55	.13				450	.11	.01
	2352	.23	.06	120	.64	.19	1814	.20	.04	153	.23	.11	4			265	.11	.04
	542	.28	.10	129	.58	.30	161	.16	.01	47	.73	.19				201	.09	.02
	2929	.22	.05	735	.48	.18	645	.15	.00	105	.30	.03	54	.07	.03	1390	.11	.01
	987	.23	.08	294	.43	.22	217	.18	.02	55	.43	.10	75	.10	.00	346	.08	.01
LOCALIZED  <i>Confirmed and Not Confirmed</i> Connecticut England and Wales <sup>2</sup> Finland <sup>3</sup>	301	.31	.11	116	.59	.27	42	.10	.00	7			4			132	.14	.01
	1490	.48	.22	686	.66	.39	345	.32	.04	96	.41	.09	8			355	.29	.06
	1606	.33	.09	121	.62	.35	672	.36	.05	89	.65	.16				724	.21	.07



France <sup>1</sup>	1137	.37	.10	.80	.73	.30	.887	.32	.05	.72	.41	.15	1	98	.22
Norway <sup>2</sup>	212	.42	.19	.66	.69	.44	.63	.19	.01	.20			6	72	.19
U.S. Central	654	.35	.14	.260	.60	.30	104	.25	.01	13			9	271	.08
U.S. Hospital	231	.41	.21	109	.63	.40	31	.17	.00	11			4	71	.03
<i>Confirmed only</i>															
Connecticut	222	.34	.13	111	.57	.26	29	.07	.00	6			4	72	.12
England and Wales <sup>2</sup>	1054	.52	.26	656	.66	.39	163	.27	.03	93	.39	.08	4	138	.27
Finland <sup>3</sup>	746	.38	.09	108	.62	.34	397	.34	.03	75	.68	.17	4	166	.17
France <sup>4</sup>	731	.38	.09	60	.72	.24	559	.33	.06	58	.42	.18	1	54	.21
Norway <sup>3</sup>	165	.48	.23	66	.69	.44	46	.18	.02	20			6	32	.22
U.S. Central	522	.39	.16	255	.60	.30	76	.26	.02	12			7	173	.13
U.S. Hospital	188	.45	.26	109	.63	.40	20			9				43	.06

Lung and Bronchus (International List No. 162.1)—Female

1945-49 ALL STAGES															
<i>Confirmed and Not Confirmed</i>															
Connecticut	174	0	.15	0	.04	.18	35	0	.20	0	.03		2	119	0
England and Wales <sup>1</sup>	862	.13	.03	.35	.32	.03	349	.17	.03	11			8	459	.07
U.S. Central	477	.18	.06	.46	.58	.23	69	.16	.05	1			4	327	.12
U.S. Hospital	86	.24	.06	.19			17			4			2	44	.16
<i>Confirmed only</i>															
Connecticut	87	.23	.06	.14			22						6	51	.12
England and Wales <sup>1</sup>	385	.13	.03	.32	.31	.16	147	.17	.01	10			2	190	.05
U.S. Central	296	.21	.06	.41	.61	.24	49	.19	.05	1			2	203	.13
U.S. Hospital	66	.22	.07	.19			14			4			2	27	.08

See footnotes at end of Appendix table.

## SURVIVAL TABLES

*One- and five-year relative survival rates by stage of disease, confirmation of diagnosis, and method of treatment. (Relative survival rates are obtained by adjusting observed rates for normal life expectancy in each country)—Continued*

Registry and period of diagnosis	Total, treated and untreated cases		Surgery		Radiation		Surgery and radiation		Chemo/hormones only		No known first course of therapy	
	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates
		1 year		5 years		1 year		5 years		1 year		5 years
Lung and Bronchus (International List No. 162.1)—Female—Continued												
1945-49												
LOCALIZED												
Confirmed and Not Confirmed												
Connecticut	39	0.18	4	0.09	7	0.28	5	0.09	28	0.07	0.04	
England and Wales <sup>1</sup>	61	.33	16	.14	25				15			
U.S. Central	65	.31	9	.15	8				48	.21	.07	
U.S. Hospital	10		7		1				2			
Confirmed only	16		3		4				9			
Connecticut	38	.32	14	.11	15		5		4			
England and Wales <sup>1</sup>	33	.42	8	.21	4				21			
U.S. Central	10		7		1				2			
U.S. Hospital												
1960-64												
ALL STAGES												
Confirmed and Not Confirmed												
Connecticut	227	.27	44	.11	45	.27	6	.09	2	.18	.07	
England and Wales <sup>2</sup>	1,442	.15	114	.05	574	.17	17	.04	21	.07	.01	
Finland <sup>3</sup>	277	.19	11	.08	40	.31	21	.06	205	.14	.05	

## SURVIVAL TABLES

France <sup>4</sup>	424	.29	.10	21		327	.28	.09	14		62	.26	.05
Norway <sup>3</sup>	149	.23	.11	17		30	.20	.00	3		96	.13	.03
U. S. Central	642	.26	.10	124	.55	.28	.23	.04	17		365	.16	.06
U. S. Hospital	119	.26	.11	23			.30	.04	7		48	.20	.05
<i>Confirmed only</i>													
Connecticut	183	.25	.10	42	.56	.25	.21	.08	6		73	.09	.02
England and Wales <sup>2</sup>	782	.16	.06	103	.42	.26	.17	.04	17		331	.06	.01
Finland <sup>2</sup>	81	.21	.09	8					17		34	.05	.00
France <sup>4</sup>	206	.29	.10	14			.30	.09	9		19		
Norway <sup>3</sup>	98	.28	.14	17					3		53	.12	.00
U. S. Central	499	.25	.09	122	.55	.28	.22	.02	17		256	.10	.02
U. S. Hospital	91	.25	.10	23					6		31	.13	.00
<i>LOCALIZED</i>													
<i>Confirmed and Not Confirmed</i>													
Connecticut	49	.38	.25	18					1		26	.16	.11
England and Wales <sup>2</sup>	138	.41	.22	57	.57	.39	.41	.20	9		35	.18	.00
Finland <sup>2</sup>	129	.27	.12	6					12		93	.18	.09
France <sup>4</sup>	113	.41	.21	3			.40	.20	5		10		
Norway <sup>3</sup>	44	.35	.22	10					2		25	.17	.00
U. S. Central	113	.41	.31	40	.71	.59			1		56	.21	.13
U. S. Hospital	16			7					1		3		
<i>Confirmed only</i>													
Connecticut	33	.47	.32	17					1		12		
England and Wales <sup>2</sup>	98	.39	.20	51	.52	.35			9		20		
Finland <sup>2</sup>	36	.27	.13	4					10		12		
France <sup>4</sup>	56	.41	.24	2					3		4		
Norway <sup>3</sup>	24			10					2		7		
U. S. Central	86	.46	.36	39	.73	.61			1		36	.13	.08
U. S. Hospital	12			7					2				

See footnotes at end of Appendix table.

*One- and five-year relative survival rates by stage of disease, confirmation of diagnosis, and method of treatment. (Relative survival rates are obtained by adjusting observed rates for normal life expectancy in each country)—Continued*

Registry and period of diagnosis	Total, treated and untreated cases		Surgery		Radiation		Surgery and radiation		Chemo/hormones only		No known first course of therapy			
	Total num-ber of cases	Relative sur-vival rates	Total num-ber of cases	Relative sur-vival rates	Total num-ber of cases	Relative sur-vival rates	Total num-ber of cases	Relative sur-vival rates	Total num-ber of cases	Relative sur-vival rates	Total num-ber of cases	Relative sur-vival rates		
													1 year	5 years
Female Breast (International List No. 170)														
1945-49														
ALL STAGES														
Confirmed and Not Confirmed														
Connecticut	2,942	0.86	0.55	2,087	0.92	0.63	95	0.47	0.05	572	0.89	0.50		
England and Wales <sup>1</sup>	10,884	.79	.44	1,968	.88	.64	2,693	.64	.20	5,284	.91	.52		
U.S. Central	7,297	.85	.55	4,720	.93	.65	456	.60	.17	1,309	.89	.51		
U.S. Hospital	1,664	.84	.48	817	.92	.61	290	.66	.20	430	.87	.44		
Confirmed only														
Connecticut	2,705	.90	.58	2,035	.92	.63	45	.46	.00	559	.90	.50		
England and Wales <sup>1</sup>	6,909	.89	.53	1,817	.89	.65	356	.68	.24	4,633	.91	.52		
U.S. Central	6,496	.89	.58	4,658	.93	.65	267	.62	.19	1,293	.89	.51		
U.S. Hospital	1,371	.88	.53	806	.92	.61	102	.75	.31	422	.87	.44		
LOCALIZED														
Confirmed and Not Confirmed														
Connecticut	1,315	.95	.76	1,083	.97	.79	14			189	.93	.67		
England and Wales <sup>1</sup>	3,255	.95	.70	951	.95	.80	240	.91	.52	1,979	.96	.67		
U.S. Central	2,891	.96	.78	2,340	.98	.81	68	.86	.42	360	.95	.70		
U.S. Hospital	489	.99	.89	361	.99	.89	16			86	.98	.94		
Confirmed only														
Connecticut	1,276	.96	.77	1,075	.97	.79	7			183	.93	.68		
England and Wales <sup>1</sup>	2,667	.96	.71	881	.95	.81	57	.89	.55	1,719	.96	.67		
U.S. Central	2,768	.97	.79	2,326	.98	.81	45	.88	.45	353	.95	.70		
U.S. Hospital	459	.99	.90	357	.99	.90	10			85	.98	.94		
											168		0.29	0.10
											20		0.46	0.14
											294		0.36	.09
											11			
											9			
											43		.52	.05
											70		.48	.13
											7			
											34		.62	.39
											2			
											15			
											11			
											1			
											1			
											6			
											10			
											9			
											38		.75	.53
											7			



*Confirmed and Not Confirmed*

Connecticut  
England and Wales <sup>2</sup>  
Finland <sup>3</sup>  
France <sup>6</sup>  
Norway <sup>3</sup>  
U.S. Central  
U.S. Hospital  
*Confirmed only*  
Connecticut  
England and Wales <sup>2</sup>  
Finland <sup>3</sup>  
France <sup>6</sup>  
Norway <sup>3</sup>  
U.S. Central  
U.S. Hospital

LOCALIZED

*Confirmed and Not Confirmed*

Connecticut  
England and Wales <sup>2</sup>  
Finland <sup>3</sup>  
France <sup>6</sup>  
Norway <sup>3</sup>  
U.S. Central  
U.S. Hospital  
*Confirmed only*  
Connecticut  
England and Wales <sup>2</sup>  
Finland <sup>3</sup>  
France <sup>4</sup>  
Norway <sup>3</sup>  
U.S. Central  
U.S. Hospital

See footnotes at end of Appendix table.

SURVIVAL TABLES

3,616	.88	.56	2,710	.93	.63	110	.46	.03	.612	.90	.48	36	.41	.04	148	.35	.07
14,040	.82	.48	2,902	.91	.67	3,373	.66	.21	6,045	.92	.56	43	.56	.11	677	.36	.15
2,401	.84	.52	415	.86	.55	145	.63	.30	1,672	.90	.56	17			152	.39	.16
3,372	.87	.57	276	.71	.47	142	.59	.15	2,735	.94	.63	43	.43	.10	176	.26	.03
8,765	.88	.58	6,025	.94	.68	436	.58	.13	1,539	.91	.51	227	.53	.12	538	.45	.17
1,784	.87	.52	1,016	.94	.65	180	.66	.11	454	.90	.47	40	.44	.05	94	.61	.33
3,417	.90	.58	2,672	.93	.64	64	.40	.03	605	.90	.48	17			59	.28	.13
9,719	.89	.57	2,760	.92	.68	632	.70	.30	6,150	.92	.56	39	.50	.19	138	.39	.25
2,178	.87	.54	386	.86	.56	100	.71	.37	1,634	.90	.56	7			51	.52	.19
3,145	.90	.60	271	.72	.47	98	.68	.20	2,726	.94	.63	16			34	.19	.07
8,190	.90	.60	5,982	.94	.68	304	.59	.14	1,530	.91	.51	158	.55	.16	216	.46	.22
1,630	.90	.56	1,011	.94	.65	103	.71	.14	451	.90	.48	26	.39	.08	39	.62	.41
1,563	.97	.79	1,394	.99	.82	12			129	.95	.67	2			26	.41	.16
4,803	.96	.72	1,627	.97	.81	326	.89	.51	2,724	.97	.70	23			103	.82	.68
1,634	.95	.71	193	.95	.69	45	.87	.59	765	.97	.73	1			30	.67	.45
1,504	.97	.80	151	.87	.66	16			1,317	.99	.82	1			19		
3,601	.98	.82	3,063	.99	.85	55	.86	.40	311	.97	.76	21			121	.63	.38
662	.97	.81	467	.99	.86	13			100	.93	.70	1			21		
1,539	.98	.70	1,391	.99	.81	6			127	.95	.67	1			14		
4,270	.96	.74	1,557	.97	.81	103	.88	.60	2,569	.97	.70	5			36	.82	.68
974	.96	.72	180	.96	.70	38	.89	.63	718	.97	.73	8			8		
2,612		.74	770		.86	585		.66	1,160		.72	27			70		
1,486	.97	.81	151	.87	.66	14			1,316	.99	.82	5			5		
3,509	.98	.83	3,068	.99	.85	40	.86	.41	369	.98	.76	15			57	.64	.47
587	.98	.82	465	.99	.86	8			99	.94	.70	15			15		

## SURVIVAL TABLES

*One- and five-year relative survival rates by stage of disease, confirmation of diagnosis, and method of treatment. (Relative survival rates are obtained by adjusting observed rates for normal life expectancy in each country)—Continued*

Registry and period of diagnosis	Total, treated and untreated cases		Surgery		Radiation		Surgery and radiation		Chemo/hormones only		No known first course of therapy	
	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates
		1 year		5 years		1 year		5 years		1 year		5 years
Uterine Cervix International List No. 171												
1945-49												
ALL STAGES												
<i>Confirmed and Not Confirmed</i>												
Connecticut	1,077	0.80	0.52		733	0.81	0.48		1		73	0.24
Denmark	2,979	.79	.53		2,582	.81	.55				201	.48
England and Wales <sup>1</sup>	5,396	.68	.38		4,301	.71	.39		3		413	.14
France	5,573	.76	.43		4,872	.76	.43		6		470	.68
U.S. Central	3,477	.76	.48		2,455	.79	.47		40	0.31	438	.45
U.S. Hospital	1,798	.79	.49		1,554	.80	.50		1		84	.46
<i>Confirmed only</i>												
Connecticut	1,007	.82	.54		693	.81	.48		1		47	.28
Denmark	2,854	.80	.53		2,516	.82	.55				150	.36
England and Wales <sup>1</sup>	4,448	.73	.41		3,698	.73	.40		1		106	.19
France	4,624	.76	.43		4,187	.77	.43		2		240	.61
U.S. Central	3,184	.78	.49		2,290	.80	.47		27	.38	339	.49
U.S. Hospital	1,775	.79	.49		1,536	.80	.50		1		81	.48
LOCALIZED												
<i>Confirmed and Not Confirmed</i>												
Connecticut	675	.88	.65		454	.86	.57				21	
Denmark	977	.92	.72		841	.92	.73				50	.83
												.72

England and Wales <sup>1</sup>	2,436	.86	.55	106	.81	.57	2,021	.87	.55	285	.86	.56	2	165	.70	.53
France	2,894	.85	.56	49	.93	.69	2,476	.85	.55	141	.91	.73	3	114	.80	.61
U.S. Central	1,710	.90	.65	238	.97	.85	1,228	.88	.61	125	.96	.78	5	21		
U.S. Hospital	583	.93	.75	30	101	.90	505	.93	.74	26	101	.96	1			
<i>Confirmed only</i>																
Connecticut	644	.89	.66	115	.98	.91	432	.87	.57	83	.96	.78		14		
Denmark	932	.92	.72	25	.85	.75	813	.93	.73	57	.90	.58		37	.82	.66
England and Wales <sup>1</sup>	2,189	.87	.55	98	.79	.57	1,811	.87	.55	272	.86	.56	1	7		
France	2,402	.85	.56	43	.94	.72	2,144	.85	.55	121	.89	.69	1	93	.79	.50
U.S. Central	1,613	.90	.66	237	.97	.85	1,149	.89	.61	124	.96	.78	5	98	.82	.68
U.S. Hospital	577	.93	.75	30	101	.90	499	.92	.74	26	101	.96	1	21		
<i>1950-54</i>																
ALL STAGES																
<i>Confirmed and Not Confirmed</i>																
Connecticut	1,069	.83	.56	203	.93	.81	694	.81	.50	128	.88	.61		44	.38	.11
Denmark	3,568	.83	.60	286	.90	.80	2,790	.84	.61	285	.84	.38		207	.51	.46
England and Wales <sup>2</sup>	5,580	.71	.42	344	.78	.62	4,180	.74	.41	669	.82	.56	13	374	.14	.03
Finland <sup>3</sup>	1,387	.79	.51	43	.84	.60	1,121	.79	.52	142	.92	.65		81	.43	.18
France	3,802	.75	.50	144	.76	.59	2,700	.74	.47	752	.82	.59	21	185	.59	.36
Norway <sup>3</sup>	1,273	.80	.52	21			989	.79	.47	216	.96	.78		47	.17	.06
U.S. Central	3,697	.82	.60	690	.95	.85	2,413	.82	.55	304	.89	.65	12	278	.48	.34
U.S. Hospital	1,627	.85	.56	102	.95	.78	1,313	.85	.56	143	.88	.57	2	67	.53	.15
<i>Confirmed only</i>																
Connecticut	1,039	.83	.56	196	.93	.80	682	.81	.50	127	.88	.62		34	.36	.13
Denmark	3,424	.83	.60	267	.89	.79	2,710	.85	.61	281	.84	.38		166	.53	.48
England and Wales <sup>2</sup>	4,999	.74	.44	326	.78	.61	3,825	.75	.42	653	.81	.56	12	183	.18	.06
Finland <sup>3</sup>	1,324	.80	.52	41	.83	.61	1,091	.80	.52	141	.93	.65		51	.45	.13
France	3,305	.76	.51	104	.75	.58	2,406	.75	.49	659	.83	.59	13	123	.61	.37
Norway <sup>3</sup>	1,249	.81	.53	21			984	.79	.47	216	.96	.78		28	.17	.10
U.S. Central	3,585	.83	.60	683	.95	.85	2,355	.82	.55	303	.89	.65	11	233	.50	.36
U.S. Hospital	1,605	.85	.56	102	.95	.78	1,301	.86	.56	143	.88	.57	2	57	.53	.15

See footnotes at end of Appendix table.

## SURVIVAL TABLES

*One- and five-year relative survival rates by stage of disease, confirmation of diagnosis, and method of treatment. (Relative survival rates are obtained by adjusting observed rates for normal life expectancy in each country)—Continued*

Registry and period of diagnosis	Total, treated and untreated cases		Surgery		Radiation		Surgery and radiation		Chemo/hormones only		No known first course of therapy					
	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates				
	1 year	5 years	1 year	5 years	1 year	5 years	1 year	5 years	1 year	5 years	1 year	5 years				
Uterine Cervix International List No. 171—Continued																
<i>1960-64</i> LOCALIZED																
	<i>Confirmed and Not Confirmed</i>															
	Connecticut	661	0.91	0.70	164	0.96	0.86	401	0.90	0.66	78	0.90	0.71	18	0.82	0.75
	Denmark	1,126	.94	.78	211	.97	.91	734	.95	.78	108	.88	.56	73	.49	.23
	England and Wales 2	2,777	.86	.59	228	.90	.78	2,053	.86	.56	458	.88	.66	29	.79	.43
	Finland 3	983	.88	.60	36	.83	.66	794	.87	.59	126	.95	.69	27	.81	.62
	France	1,958	.87	.68	86	.90	.70	1,327	.85	.66	460	.91	.75	75	.76	.56
	Norway 3	337	.97	.79	3			167	.95	.70	166	.98	.87	1	.76	.56
	U.S. Central	2,004	.93	.77	544	.99	.92	1,166	.91	.72	186	.94	.78	103	.76	.56
	U.S. Hospital	690	.95	.77	74	100	.94	526	.96	.77	67	.94	.76	23	.76	.56
	<i>Confirmed only</i>															
Connecticut	648	.91	.70	157	.96	.85	397	.90	.66	78	.90	.71	16	.82	.74	
Denmark	1,064	.94	.78	193	.97	.91	702	.95	.78	107	.89	.56	62	.82	.74	
England and Wales 2	2,626	.87	.60	214	.90	.77	1,934	.86	.56	446	.88	.66	23	.81	.67	
Finland 3	953	.88	.60	34	.82	.67	775	.87	.59	126	.95	.69	18	.76	.56	
France	1,728	.87	.68	62	.86	.67	1,203	.85	.66	409	.92	.74	3	.76	.56	
Norway 3	337	.97	.79	3			167	.95	.70	166	.98	.87	1	.76	.54	
U.S. Central	1,971	.93	.77	537	.99	.92	1,147	.91	.72	186	.94	.78	96	.76	.54	
U.S. Hospital	685	.95	.77	74	100	.94	524	.96	.77	67	.94	.76	20	.76	.54	



## SURVIVAL TABLES

421

Uterine Corpus (International List Nos. 172 and 174)

1945-49 ALL STAGES																	
Confirmed and Not Confirmed																	
Confirmed only	Connecticut	910	0.82	0.64	337	0.89	0.77	173	0.78	0.36	273	0.91	0.74		77	0.21	0.07
	Denmark	1,033	.83	.61	266	.87	.81	537	.84	.55	159	.89	.58		71	.42	.40
	England and Wales 1	1,142	.76	.55	413	.89	.75	393	.72	.37	225	.87	.68	1	110	.18	.11
	France	285	.73	.48	97	.85	.69	109	.67	.32	22			1	56	.56	.20
	U.S. Central	2,047	.79	.62	750	.88	.76	569	.80	.51	419	.89	.72	21	288	.43	.35
	U.S. Hospital	512	.86	.63	88	.92	.75	225	.81	.50	172	.91	.74		27	.72	.49
LOCALIZED	Connecticut	840	.85	.66	376	.89	.78	157	.80	.37	269	.91	.74		38	.28	.07
	Denmark	966	.84	.62	248	.86	.82	513	.84	.55	152	.90	.60		53	.45	.40
	England and Wales 1	1,017	.80	.58	399	.90	.76	344	.73	.37	216	.87	.68	1	57	.22	.12
	France	189	.77	.51	72	.87	.75	71	.70	.31	18			1	27	.49	.00
	U.S. Central	1,877	.83	.65	739	.88	.76	623	.81	.52	415	.89	.72	18	182	.53	.41
	U.S. Hospital	505	.86	.63	88	.92	.75	221	.81	.50	171	.91	.74		25	.73	.52
LOCALIZED																	
Confirmed and Not Confirmed																	
Confirmed only	Connecticut	628	.93	.77	305	.95	.86	111	.88	.46	197	.97	.83		15		.57
	Denmark	740	.91	.72	226	.90	.85	377	.92	.66	101	.96	.67		36	.62	
	England and Wales 1	591	.89	.69	252	.95	.81	203	.83	.50	125	.92	.74		11		
	France	185	.81	.60	84	.87	.74	55	.80	.45	13			1	32	.55	.33
	U.S. Central	1,280	.91	.78	560	.94	.86	346	.88	.64	287	.95	.83	6	81	.72	.63
	U.S. Hospital	301	.94	.81	53	.96	.88	123	.93	.70	108	.96	.94		17		
LOCALIZED	Connecticut	611	.94	.78	302	.95	.86	104	.89	.46	196	.97	.83		9		
	Denmark	709	.90	.71	213	.89	.85	363	.92	.65	100	.96	.68		33	.59	.52
	England and Wales 1	551	.90	.70	243	.95	.82	181	.84	.50	119	.91	.75		8		
	France	122	.85	.64	60	.90	.82	35	.85	.40	10			1	16		
	U.S. Central	1,249	.92	.78	557	.94	.86	331	.88	.63	286	.95	.83	6	69	.79	.69
	U.S. Hospital	206	.94	.81	53	.96	.88	120	.92	.69	107	.96	.94		16		

See footnotes at end of Appendix table.

*One- and five-year relative survival rates by stage of disease, confirmation of diagnosis, and method of treatment. (Relative survival rates are obtained by adjusting observed rates for normal life expectancy in each country)—Continued*

Registry and period of diagnosis	Total treated and untreated cases		Surgery		Radiation		Surgery and radiation		Chemo/hormones only		No known first course of therapy				
	Total num-ber of cases	Relative sur-vival rates 1 year 5 years	Total num-ber of cases	Relative sur-vival rates 1 year 5 years	Total num-ber of cases	Relative sur-vival rates 1 year 5 years	Total num-ber of cases	Relative sur-vival rates 1 year 5 years	Total num-ber of cases	Relative sur-vival rates 1 year 5 years	Total num-ber of cases	Relative sur-vival rates 1 year 5 years			
Uterine Corpus (International List Nos. 172 and 174)—Continued															
1950-54 ALL STAGES															
<i>Confirmed and Not Confirmed</i>															
Connecticut	1,122	0.86	0.72	493	0.91	0.81	208	0.74	0.51	366	0.94	0.78	55	0.29	0.16
Denmark	1,318	.85	.68	481	.90	.85	538	.86	.62	230	.88	.54	69	.36	.36
England and Wales <sup>2</sup>	1,935	.82	.66	895	.91	.80	439	.75	.43	458	.91	.75	141	.18	.14
Finland <sup>3</sup>	822	.81	.67	134	.84	.79	218	.81	.61	387	.91	.75	83	.29	.12
France	557	.72	.49	169	.85	.75	227	.65	.37	100	.80	.53	58	.44	.07
Norway <sup>3</sup>	675	.75	.59	113	.82	.66	92	.63	.30	364	.92	.76	106	.17	.00
U.S. Central	2,479	.85	.71	975	.92	.82	536	.77	.51	777	.93	.79	182	.38	.27
U.S. Hospital	574	.87	.70	122	.95	.78	150	.70	.45	281	.94	.82	21		
<i>Confirmed only</i>															
Connecticut	1,093	.87	.73	488	.91	.81	205	.75	.51	365	.94	.78	35	.37	.22
Denmark	1,265	.86	.68	462	.90	.85	521	.86	.62	226	.87	.53	56	.36	.32
England and Wales <sup>2</sup>	1,800	.85	.68	867	.91	.80	396	.75	.44	446	.92	.76	90	.23	.18
Finland <sup>3</sup>	757	.85	.70	132	.83	.80	207	.82	.63	382	.92	.76	36	.43	.20
France	463	.74	.51	146	.87	.77	198	.66	.37	89	.82	.57	2		
Norway <sup>3</sup>	615	.80	.63	112	.83	.67	92	.63	.30	364	.92	.76	28	.44	.00
U.S. Central	2,412	.86	.72	970	.92	.82	523	.77	.51	776	.93	.79	47	.16	.00
U.S. Hospital	568	.87	.70	120	.96	.79	149	.70	.44	280	.94	.82	135	.46	.34

## LOCALIZED

*Confirmed and Not Confirmed*

Connecticut	840	.93	.83	401	.96	.88	131	.86	.65	287	.97	.86	21	.58	.59
Denmark	943	.94	.79	382	.96	.92	388	.93	.72	148	.95	.64	25		
England and Wales <sup>2</sup>	1,240	.93	.79	672	.95	.85	236	.86	.56	308	.96	.82	24		
Finland <sup>3</sup>	660	.91	.77	117	.91	.87	179	.87	.71	339	.95	.80	25	.71	.36
France	391	.80	.61	147	.87	.78	138	.77	.50	72	.81	.62	32	.59	.14
Norway <sup>3</sup>	492	.88	.73	91	.90	.75	54	.80	.44	322	.94	.81	25	.15	.00
U.S. Central	1,689	.94	.85	748	.97	.90	313	.87	.66	563	.98	.89	65	.65	.57
U.S. Hospital	378	.96	.86	82	.98	.91	77	.88	.65	207	1.00	.93	12		
<i>Confirmed only</i>															
Connecticut	836	.93	.83	399	.96	.88	130	.86	.65	287	.97	.86	20		
Denmark	910	.93	.79	367	.96	.92	376	.93	.72	144	.95	.63	23		
England and Wales <sup>2</sup>	1,185	.93	.79	650	.95	.85	214	.86	.58	302	.96	.82	19		
Finland <sup>3</sup>	645	.92	.78	116	.91	.87	175	.88	.72	337	.95	.80	17		
France	332	.82	.63	130	.89	.79	123	.77	.50	64	.82	.66	14		
Norway <sup>3</sup>	480	.90	.74	91	.90	.75	54	.80	.44	322	.94	.81	13		
U.S. Central	1,677	.94	.85	746	.97	.90	308	.87	.66	563	.98	.89	60	.67	.58
U.S. Hospital	377	.96	.86	81	.97	.91	77	.88	.65	207	1.00	.93	12		

## Ovary (International List No. 175.0)

1945-49  
ALL STAGES*Confirmed and Not Confirmed*

Connecticut	597	0.49	0.25	260	0.62	0.39	63	0.32	0.02	125	0.70	0.36	2	0.14	0.01
England and Wales <sup>1</sup>	1,420	.40	.21	420	.52	.33	153	.32	.09	379	.69	.33	5	.09	.02
U.S. Central	1,369	.48	.26	603	.65	.39	144	.26	.02	247	.73	.39	29	.13	.02
U.S. Hospital	251	.51	.29	68	.61	.43	41	.32	.03	95	.70	.41	47	.14	.05
<i>Confirmed only</i>															
Connecticut	544	.52	.27	251	.64	.40	62	.33	.02	122	.71	.36	2	.17	.01
England and Wales <sup>1</sup>	1,385	.46	.24	387	.53	.33	89	.36	.07	347	.68	.32	3	.08	.01
U.S. Central	1,253	.51	.27	593	.65	.40	118	.27	.02	244	.73	.39	25	.14	.01
U.S. Hospital	233	.54	.30	66	.59	.42	34	.39	.03	94	.71	.42	39	.16	.06

See footnotes at end of Appendix table.

*One- and five-year relative survival rates by stage of disease, confirmation of diagnosis, and method of treatment. (Relative survival rates are obtained by adjusting observed rates for normal life expectancy in each country)—Continued*

Registry and period of diagnosis	Total treated and untreated cases		Surgery		Radiation		Surgery and radiation		Chemo/hormones only		No known first course of therapy			
	Total num-ber of cases	Relative sur-vival rates 1 year 5 years	Total num-ber of cases	Relative sur-vival rates 1 year 5 years	Total num-ber of cases	Relative sur-vival rates 1 year 5 years	Total num-ber of cases	Relative sur-vival rates 1 year 5 years	Total num-ber of cases	Relative sur-vival rates 1 year 5 years	Total num-ber of cases	Relative sur-vival rates 1 year 5 years		
Ovary (International List No. 175.0)—Continued														
1945-49 LOCALIZED  <i>Confirmed and Not Confirmed</i> Connecticut England and Wales <sup>1</sup> U.S. Central U.S. Hospital <i>Confirmed only</i> Connecticut England and Wales <sup>1</sup> U.S. Central U.S. Hospital	168	0.78	0.60	116	0.79	0.66	3		39	0.91	0.60		10	
	312	.79	.53	156	.79	.64	3		148	.80	.44		5	
	360	.81	.62	255	.84	.65	8		78	.89	.66	1	18	
	60	.86	.80	31	.84	.78	1		27	.94	.87		1	
	165	.79	.60	114	.79	.66	3		39	.91	.60		9	
	283	.79	.54	146	.79	.63	2		132	.79	.45		3	
	355	.82	.63	253	.84	.66	8		78	.89	.66	1	15	
	59	.86	.79	30	.84	.77	1		27	.94	.87		1	
	743	.55	.31	344	.74	.48	86	0.30 0.00	161	.67	.34	1	151	0.13 0.04
	<i>Confirmed and Not Confirmed</i> Connecticut													



England and Wales <sup>2</sup>	1,984	.47	.27	.697	.65	.37	220	.23	.08	498	.74	.46	31	.26	.00	538	.08	.03
Finland <sup>3</sup>	743	.53	.33	153	.55	.41	101	.27	.13	344	.74	.44	9			136	.19	.10
France <sup>4,5</sup>	447	.43	.21															
Norway <sup>3</sup>	874	.46	.23	134	.52	.30	93	.32	.02	350	.76	.42	3			294	.11	.01
U.S. Central	1,608	.62	.28	679	.74	.46	202	.23	.02	387	.65	.30	13			327	.12	.03
U.S. Hospital	317	.52	.23	88	.72	.37	72	.27	.06	115	.63	.29	3			39	.26	.09
<i>Confirmed only</i>																		
Connecticut	692	.57	.32	337	.74	.49	79	.28	.00	157	.68	.35				119	.12	.01
England and Wales <sup>2</sup>	1,633	.52	.30	646	.66	.38	160	.20	.03	480	.74	.46	20			327	.10	.04
Finland <sup>3</sup>	579	.59	.36	141	.57	.42	47	.24	.05	332	.75	.44	5			54	.07	.03
France <sup>6</sup>																		
Norway <sup>3</sup>	724	.52	.26	131	.52	.30	65	.37	.02	349	.76	.42	2			177	.08	
U.S. Central	1,599	.54	.29	672	.74	.46	183	.22	.02	383	.66	.31	11			260	.11	.02
U.S. Hospital	296	.53	.24	.86	.71	.38	62	.26	.05	114	.63	.29	2			32	.22	.07
<i>LOCALIZED</i>																		
<i>Confirmed and Not Confirmed</i>																		
Connecticut	218	.87	.69	160	.91	.74	4			52	.79	.63				2		
England and Wales <sup>2</sup>	579	.85	.59	323	.84	.57	18			228	.89	.65	2			8		
Finland <sup>3</sup>	330	.82	.61	81	.81	.73	17			212	.87	.59				20		
France <sup>4,5</sup>	77	.72	.46															
Norway <sup>3</sup>	253	.83	.55	60	.78	.55	2			177	.91	.59	1			13		
U.S. Central	440	.85	.64	314	.90	.69	8			108	.81	.60				10		
U.S. Hospital	66	.89	.69	35	.87	.66	3			27	.97	.78				1		
<i>Confirmed only</i>																		
Connecticut	215	.87	.69	159	.90	.73	2			52	.79	.63				2		
England and Wales <sup>2</sup>	536	.85	.59	297	.84	.57	10			221	.89	.65	1			7		
Finland <sup>3</sup>	299	.84	.61	78	.81	.73	7			209	.86	.59				5		
France <sup>6</sup>																		
Norway <sup>3</sup>	242	.85	.57	60	.78	.55	1			176	.91	.50	1			4		
U.S. Central	433	.86	.65	313	.90	.69	5			108	.81	.60				7		
U.S. Hospital	66	.89	.69	35	.87	.66	3			27	.97	.78				1		

See footnotes at end of Appendix table.

*One- and five-year relative survival rates by stage of disease, confirmation of diagnosis, and method of treatment. (Relative survival rates are obtained by adjusting observed rates for normal life expectancy in each country)—Continued*

Registry and period of diagnosis	Total, treated and untreated cases		Surgery		Radiation		Surgery and radiation		Chemo/hormones only		No known first course of therapy							
	Total num-ber of cases	Relative sur-vival rates 1 year 5 years	Total num-ber of cases	Relative sur-vival rates 1 year 5 years	Total num-ber of cases	Relative sur-vival rates 1 year 5 years	Total num-ber of cases	Relative sur-vival rates 1 year 5 years	Total num-ber of cases	Relative sur-vival rates 1 year 5 years	Total num-ber of cases	Relative sur-vival rates 1 year 5 years						
Prostate (International List No. 177)																		
<i>1945-49</i> ALL STAGES  <i>Confirmed and Not Confirmed</i> Connecticut England and Wales <sup>1</sup> U.S. Central U.S. Hospital <i>Confirmed only</i> Connecticut England and Wales <sup>1</sup> U.S. Central U.S. Hospital	1,159	0.68	0.35	790	0.80	0.46	15	0.43	0.13	25	0.72	0.32	84	0.84	0.28	245	0.22	0.06
	1,603	.60	.30	743	.68	.40	77	.72	.16	28	.72	.16	505	.74	.32	250	.11	.05
	2,831	.69	.36	1,743	.81	.46	40	.56	.11	39	.65	.27	499	.66	.28	510	.31	.12
	483	.72	.38	170	.84	.49	19			7			211	.68	.35	76	.62	.28
	872	.72	.41	685	.82	.49	8			22			30	.89	.30	127	.18	.08
	686	.66	.38	557	.73	.44	20			22			30	.74	.35	57	.00	.00
	2,064	.73	.41	1,626	.82	.47	17			35	.63	.27	164	.64	.26	222	.19	.10
	289	.76	.39	164	.84	.50	15			6			78	.71	.33	26	.50	.17

1960-64  
ALL STAGES

*Confirmed and Not Confirmed*

Connecticut  
England and Wales <sup>2</sup>  
Finland <sup>3</sup>  
France <sup>4,5</sup>  
Norway <sup>3</sup>  
U.S. Central  
U.S. Hospital

*Confirmed only*

Connecticut  
England and Wales <sup>2</sup>  
Finland <sup>3</sup>  
France <sup>6</sup>  
Norway <sup>3</sup>  
U.S. Central  
U.S. Hospital

LOCALIZED

*Confirmed and Not Confirmed*

Connecticut  
England and Wales <sup>2</sup>  
Finland <sup>3</sup>  
France <sup>4,5</sup>  
Norway <sup>3</sup>  
U.S. Central  
U.S. Hospital

*Confirmed only*

Connecticut  
England and Wales <sup>2</sup>  
Finland <sup>3</sup>  
France <sup>6</sup>  
Norway <sup>3</sup>  
U.S. Central  
U.S. Hospital

See footnotes at end of Appendix table.

SURVIVAL TABLES

1,600	.72	.41	1,147	.85	.50	12	.49	.17	20			141	.69	.34	250	.23	.10
2,398	.65	.34	1,172	.73	.42	112	.68	.19	23			800	.71	.35	291	.21	.10
738	.55	.23	243	.66	.38	44			61	.75	.34	249	.52	.15	141	.24	.07
430	.54	.22															
2,086	.71	.38	924	.83	.54	97	.68	.27	42	.92	.40	741	.72	.29	282	.27	.08
3,580	.71	.40	2,227	.85	.52	46	.48	.12	59	.80	.26	633	.67	.29	615	.28	.11
636	.76	.42	299	.82	.53	11			6			200	.76	.35	60	.56	.29
1,222	.75	.45	1,004	.85	.52	7			16			38	.76	.43	157	.15	.06
1,230	.68	.39	995	.75	.45	31	.57	.28	15			106	.55	.20	83	.12	.02
305	.70	.36	170	.75	.46	16			45	.84	.42	50	.67	.21	24		
1,244	.77	.46	911	.83	.54	25	.46	.15	41	.91	.41	174	.77	.33	93	.20	.07
2,725	.74	.44	2,076	.85	.53	30	.38	.09	53	.79	.26	224	.69	.29	342	.16	.08
400	.79	.44	276	.82	.55	8			4			86	.81	.25	26	.48	.22
836	.81	.55	677	.91	.63	3			5			42	.88	.48	109	.18	.10
993	.83	.55	699	.83	.54	14			9			228	.91	.58	43	.51	.28
390	.68	.37	178	.73	.46	12			43	.80	.41	117	.63	.27	40	.44	.16
164	.68	.36															
1,225	.80	.51	768	.85	.56	45	.84	.47	28	.93	.57	283	.80	.48	101	.30	.15
1,763	.81	.56	1,353	.90	.63	6			16			149	.87	.55	239	.26	.13
293	.81	.60	177	.85	.68	2			1			96	.78	.52	17		
758	.81	.57	649	.90	.64	3			5			15			86	.08	.04
679	.83	.55	632	.84	.56	6			8			20			13		
215	.74	.45	143	.76	.50	2			36	.82	.46	27	.64	.33	7		
901	.83	.55	761	.85	.57	8			28	.93	.57	73	.86	.53	31	.18	.10
1,575	.81	.57	1,322	.90	.64	6			16			56	.88	.60	175	.11	.08
214	.82	.61	173	.85	.68	2			1			31	.75	.44	7		

*One- and five-year relative survival rates by stage of disease, confirmation of diagnosis, and method of treatment. (Relative survival rates are obtained by adjusting observed rates for normal life expectancy in each country)—Continued*

Registry and period of diagnosis	Total, treated and untreated cases		Surgery		Radiation		Surgery and radiation		Chemohormones only		No known first course of therapy		
	Total num-ber of cases	Relative sur-vival rates 1 year 5 years	Total num-ber of cases	Relative sur-vival rates 1 year 5 years	Total num-ber of cases	Relative sur-vival rates 1 year 5 years	Total num-ber of cases	Relative sur-vival rates 1 year 5 years	Total num-ber of cases	Relative sur-vival rates 1 year 5 years	Total num-ber of cases	Relative sur-vival rates 1 year 5 years	
Testis (International List No. 178)													
1945-49													
ALL STAGES													
Confirmed and Not Confirmed													
Connecticut	112	.69	.47	33	.73	.56	3	.36	.26	70	.75	.43	6
England and Wales 1	300	.64	.52	37	.61	.53	25	.36	.26	224	.72	.57	13
U.S. Central	221	.69	.46	91	.77	.53	6			102	.73	.49	22
U.S. Hospital	75	.72	.51	25	.80	.58	2			45	.72	.53	2
Confirmed only													
Connecticut	107	.71	.48	32	.75	.58	2			68	.74	.48	5
England and Wales 1	251	.69	.54	34	.63	.60	10			202	.72	.56	5
U.S. Central	210	.71	.48	90	.78	.54	5			100	.72	.49	15
U.S. Hospital	74	.72	.52	25	.80	.58	2			45	.72	.53	1
LOCALIZED													
Confirmed and Not Confirmed													
Connecticut	73	.77	.57	26	.81	.63	1			45	.78	.54	1
England and Wales 1	173	.87	.72	27	.76	.72	5			141	.89	.71	3
U.S. Central	117	.83	.61	54	.85	.66	1			59	.83	.56	3
U.S. Hospital	37	.98	.72	14						23			
Confirmed only													
Connecticut	72	.78	.57	26	.81	.63	1			45	.78	.54	
England and Wales 1	158	.86	.71	26	.75	.70	3			129	.88	.70	2
U.S. Central	116	.84	.61	54	.85	.66	1			59	.83	.56	
U.S. Hospital	37	.98	.72	14						23			



1950-54  
ALL STAGES

*Confirmed and Not Confirmed*

Connecticut	119	.72	.53	.42	.67	.47	2	.37	.32	71	.82	.60	4
England and Wales 2	386	.73	.61	53	.65	.48	33			288	.81	.68	12
Finland 3	67	.70	.52	26	.62	.50	1			34	.86	.62	6
Norway 3	216	.71	.54	37	.49	.34	3			169	.79	.61	7
U.S. Central	220	.69	.51	95	.68	.53	3			105	.83	.59	17
U.S. Hospital	86	.74	.54	22			1			60	.74	.53	1
<i>Confirmed only</i>													2
Connecticut	116	.74	.54	42	.67	.47	1			71	.82	.60	2
England and Wales 2	364	.74	.62	52	.66	.49	22			281	.81	.68	9
Finland 3	63	.72	.54	25	.60	.52	1			34	.86	.62	3
Norway 3	212	.73	.55	37	.49	.34	3			169	.79	.61	3
U.S. Central	213	.71	.53	95	.68	.53	2			105	.83	.59	11
U.S. Hospital	84	.75	.55	22			1			59	.75	.54	1

LOCALIZED

*Confirmed and Not Confirmed*

Connecticut	71	.91	.72	26	.85	.68	8			44	.96	.76	1
England and Wales 2	232	.90	.78	22						201	.91	.79	1
Finland 3	38	.85	.69	16						21			1
Norway 3	145	.93	.73	20			1			124	.94	.76	
U.S. Central	116	.93	.74	57	.92	.78				57	.97	.74	2
U.S. Hospital	47	.96	.81	13						34	.93	.84	
<i>Confirmed only</i>													
Connecticut	70	.92	.73	26	.85	.68				44	.96	.76	
England and Wales 2	223	.90	.79	22			6			195	.90	.79	
Finland 3	37	.84	.70	15						21			1
Norway 3	145	.93	.73	20			1			124	.94	.76	
U.S. Central	115	.94	.75	57	.92	.78				57	.97	.74	1
U.S. Hospital	47	.96	.81	13						34	.93	.84	

See footnotes at end of Appendix table.

## SURVIVAL TABLES

*One- and five-year relative survival rates by stage of disease, confirmation of diagnosis, and method of treatment. (Relative survival rates are obtained by adjusting observed rates for normal life expectancy in each country)—Continued*

Registry and period of diagnosis	Total, treated and untreated cases		Surgery		Radiation		Surgery and radiation		Chemo/hormones only		No known first course of therapy	
	Total num-ber of cases	Relative sur-vival rates 1 year 5 years	Total num-ber of cases	Relative sur-vival rates 1 year 5 years	Total num-ber of cases	Relative sur-vival rates 1 year 5 years	Total num-ber of cases	Relative sur-vival rates 1 year 5 years	Total num-ber of cases	Relative sur-vival rates 1 year 5 years	Total num-ber of cases	Relative sur-vival rates 1 year 5 years
Melanoma (International List No. 190)—Male												
1945-49 ALL STAGES												
Confirmed and Not Confirmed												
Connecticut	81	0.77	0.41	69	0.81	0.45	2	0.72	0.47	5		5
Denmark	150	.79	.43	95	.81	.43	31	.69	.41	2		22
England and Wales 1	178	.74	.47	90	.80	.53	35			41	0.77	0.46
U.S. Central	206	.72	.40	148	.83	.49	7			8		10
U.S. Hospital	71	.67	.30	40	.85	.51	9			7		43
Confirmed only												15
Connecticut	81	.77	.41	69	.81	.45	2			5		5
Denmark	136	.81	.42	92	.80	.42	24			2		18
England and Wales 1	142	.76	.47	81	.81	.51	16			41	.77	.46
U.S. Central	195	.72	.40	148	.83	.49	7			8		4
U.S. Hospital	71	.67	.30	40	.85	.51	9			7		32
Localized												15
Confirmed and Not Confirmed												.29
Connecticut	48	.93	.58	41	.94	.62	2			3		.08
Denmark 6												2



One- and five-year relative survival rates by stage of disease, confirmation of diagnosis, and method of treatment. (Relative survival rates are obtained by adjusting observed rates for normal life expectancy in each country)—Continued

Registry and period of diagnosis	Total, treated and untreated cases		Surgery		Radiation		Surgery and radiation		Chemo/hormones only		No known first course of therapy	
	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates
	1 year	5 years	1 year	5 years	1 year	5 years	1 year	5 years	1 year	5 years	1 year	5 years
Melanoma (International List No. 190)—Male—Continued												
1950-54												
LOCALIZED												
Confirmed and Not Confirmed												
Connecticut	65	0.96	0.58		64	0.96	0.59	1				
Denmark <sup>6</sup>											1	
England and Wales <sup>2</sup>	93	.90	.61		74	.90	.62	8				
Finland <sup>3</sup>	50	.94	.58		11			6	10	0.99	0.58	
France <sup>4, 6</sup>	133	.85	.54						33			
Norway <sup>3</sup>	81	.93	.59	23					58	.95	.60	
U.S. Central	156	.93	.63	149		.94	.64	1	1			5
U.S. Hospital	30	.89	.66	28		.92	.70					2
Confirmed only												
Connecticut	64	.96	.59		63	.96	.60	1				
Denmark <sup>6</sup>												
England and Wales <sup>2</sup>	78	.90	.60		64	.88	.60	4	9	.99	.59	1
Finland <sup>3</sup>	49	.94	.59	11				6	32			
France <sup>6</sup>												
Norway <sup>3</sup>	81	.93	.59	23					58	.95	.60	5
U.S. Central	153	.92	.62	146		.94	.64	1	1			2
U.S. Hospital	30	.89	.66	28		.92	.70					



Melanoma (International List No. 190)—Female

1945-49 ALL STAGES		Confirmed and Not Confirmed		Confirmed only		LOCALIZED		Confirmed and Not Confirmed		Confirmed only	
Connecticut	99	.85	.60	.95	.86	.61					
Denmark	180	.84	.60	121	.89	.63					
England and Wales †	228	.84	.58	125	.95	.70					
U.S. Central	238	.81	.56	132	.85	.60					
U.S. Hospital	48	.81	.58	40	.87	.63					
Confirmed only											
Connecticut	97	.84	.60	94	.86	.62					
Denmark	154	.84	.58	111	.88	.61					
England and Wales †	178	.83	.58	110	.94	.70					
U.S. Central	213	.81	.56	130	.85	.60					
U.S. Hospital	47	.83	.60	39	.89	.65					
LOCALIZED											
Confirmed and Not Confirmed											
Connecticut	74	.96	.73	72	.96	.74					
Denmark †											
England and Wales †	152	.96	.72	95	.97	.76					
U.S. Central	160	.94	.71	141	.93	.71					
U.S. Hospital	22			20							
Confirmed only											
Connecticut	73	.96	.73	72	.96	.74					
Denmark †											
England and Wales †	117	.94	.70	80	.96	.78					
U.S. Central	148	.93	.70	140	.93	.70					
U.S. Hospital	22			20							

See footnotes at end of Appendix table.

*One- and five-year relative survival rates by stage of disease, confirmation of diagnosis, and method of treatment. (Relative survival rates are obtained by adjusting observed rates for normal life expectancy in each country)—Continued*

Registry and period of diagnosis	Total, treated and untreated cases			Surgery			Radiation			Surgery and radiation			Chemo/hormones only			No known first course of therapy			
	Total num-ber of cases	Relative sur-vival rates		Total num-ber of cases	Relative sur-vival rates		Total num-ber of cases	Relative sur-vival rates		Total num-ber of cases	Relative sur-vival rates		Total num-ber of cases	Relative sur-vival rates		Total num-ber of cases	Relative sur-vival rates		
		1 year	5 years		1 year	5 years		1 year	5 years		1 year	5 years		1 year	5 years				
Melanoma (International List No. 190)—Female—Continued																			
1950-54 ALL STAGES  <i>Confirmed and Not Confirmed</i>	145	0.85	0.61	136	0.90	0.64	1			2						6			
	252	.80	.59	186	.85	.65	32	0.71	0.38	4						30	0.62	0.42	
	336	.87	.51	242	.93	.57	33	.80	.39	36	0.82	0.38				25	.51	.16	
	151	.81	.48	29	.80	.56	16			91	.92	.52				15			
	353	.79	.53																
	166	.86	.54	48	.88	.50	6			108	.88	.57				4			
	372	.84	.62	326	.91	.67	2			8						32	.34	.20	
	78	.69	.46	61	.82	.57	1			1						14			
	<i>Confirmed only</i>																		
	139	.85	.61	132	.90	.64	1			2						4			
	214	.80	.59	166	.86	.65	22			3						23			
	282	.88	.51	222	.92	.56	14			33	.81	.35				13			
	149	.81	.49	29	.80	.56	16			91	.92	.52				13			
	France <sup>6</sup>																		
	Norway <sup>5</sup>	164	.85	.53	48	.88	.50	4			108	.88	.57				4		
	U.S. Central	360	.84	.62	321	.91	.67	2			8						25	.21	.09
	U.S. Hospital	77	.70	.46	61	.82	.57	1			1						13		

LOCALIZED  
Confirmed and Not Confirmed

Connecticut	106	.98	.73	105	.98	.72	20	21	.98	.63	1	1
Denmark <sup>6</sup>	226	.98	.61	173	.99	.65	7	61	.98		12	4
England and Wales <sup>2</sup>	91	.93	.61	19				82	.95	.71	3	2
Finland <sup>2</sup>	228	.89	.68	36	.96	.56	2	3				
France <sup>4 5</sup>	120	.96	.68	237	.98	.78						
Norway <sup>2</sup>	244	.98	.79	35	.91	.82						
U.S. Central	37	.92	.81	103	.98	.73						
U.S. Hospital												
Confirmed only												
Connecticut	103	.98	.73	103	.98	.73						
Denmark <sup>6</sup>	188	.98	.61	156	.99	.64	7	19	.98	.63	6	3
England and Wales <sup>2</sup>	90	.94	.62	19			7	61				
Finland <sup>2</sup>												
France <sup>6</sup>												
Norway <sup>2</sup>	119	.96	.67	36	.96	.56	1	82	.95	.71	1	1
U.S. Central	230	.98	.79	234	.98	.79		3			2	2
U.S. Hospital	37	.92	.81	35	.91	.82						

See footnotes at end of Appendix table.

## SURVIVAL TABLES

*One- and two-year relative survival rates by confirmation of diagnosis and method of treatment. (Relative survival rates are obtained by adjusting observed rates for normal life expectancy in each country)*

Registry and period of diagnosis	Total, treated and untreated cases <sup>1</sup>		Radiation only		Radiation with chemo/hormones		Radiation with or without chemo/hormones		Chemo/hormones only		No known first course of therapy	
	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates
	1 year	2 years	1 year	2 years	1 year	2 years	1 year	2 years	1 year	2 years	1 year	2 years
Leukemia Summary (International List No. 294)—Male												
1945-49												
<i>All Leukemias Specified as Acute</i>												
Connecticut	111	0.05	0.03	17	1		18		12		56	0.02
Denmark	110	.02	.01	16	3		16		24		92	.00
England and Wales <sup>1</sup>	182	.05	.03	35	0.17	0.12	38	0.19	26	0.08	120	.01
U.S. Central	243	.04	.02	36	.08	.06	40	.10	26	.02	151	.01
U.S. Hospital	104	.03	.00	34	.06	.00	35	.06	19	.00	48	.00
<i>All Leukemias Not Specified as Acute</i>												
Connecticut	228	.45	.32	75	.56	.39	79	.56	11		113	.34
Denmark	518	.35	.25	220	.58	.42	220	.58	12		295	.18
England and Wales <sup>1</sup>	386	.52	.35	250	.58	.37	281	.59	12		90	.32
U.S. Central	517	.42	.28	169	.57	.38	178	.56	21		291	.31
U.S. Hospital	172	.44	.28	85	.61	.37	90	.59	14		68	.23
<i>Total of All Leukemias</i>												
Connecticut	339	.32	.22	92	.48	.33	97	.49	23		169	.23
Denmark	628	.29	.21	236	.54	.40	236	.54	36	.11	387	.14
England and Wales <sup>1</sup>	508	.36	.24	285	.53	.34	319	.54	47	.09	210	.14
U.S. Central	760	.29	.20	205	.49	.32	218	.48	33	.15	442	.21
U.S. Hospital	276	.29	.17	119	.45	.26	125	.44	33	.24	116	.13



## SURVIVAL TABLES

1950-54														
<i>All Leukemias Specified as Acute</i>														
Connecticut	142	.18	.06	12	3			15	42	.22	.07	84	.16	.04
Denmark	186	.04	.03	18				18				165	.02	.02
England and Wales <sup>2</sup>	295	.04	.02	29	9	.07		38	.08	.08	.00	161	.03	.01
Finland <sup>3</sup>	175	.03	.01	3	3			6			.01	32	.00	.00
Norway <sup>3</sup>	266	.06	.01	4	3			7			.02	122	.03	.00
U.S. Central	312	.14	.04	24	8			32	.10	.07	.04	178	.13	.04
U.S. Hospital	153	.13	.04	3	7			10			.03	25	.12	.08
<i>All Leukemias Not Specified as Acute</i>														
Connecticut	278	.50	.40	74	7	.56	.43	81	.56	.45	.34	159	.48	.39
Denmark	555	.39	.26	219		.55	.38	219	.55	.38	.17	323	.27	.17
England and Wales <sup>2</sup>	629	.53	.35	305	96	.58	.40	401	.63	.43	.10	162	.36	.22
Finland <sup>3</sup>	218	.32	.20	29	16	.25	.15	45	.32	.19	.21	24		
Norway <sup>3</sup>	261	.47	.29	52	14	.73	.40	66	.70	.38	.36	115	.33	.19
U.S. Central	599	.48	.37	155	23	.59	.47	178	.55	.45	.23	342	.46	.36
U.S. Hospital	215	.58	.40	87	14	.76	.52	101	.76	.52	.26	54	.42	.31
<i>Total of All Leukemias</i>														
Connecticut	420	.39	.28	86	10	.51	.39	96	.50	.39	.19	243	.37	.27
Denmark	741	.30	.20	237		.52	.36	237	.52	.36		488	.18	.11
England and Wales <sup>2</sup>	924	.37	.24	334	105	.54	.37	439	.58	.40	.03	323	.19	.11
Finland <sup>3</sup>	393	.19	.11	32	19	.22	.13	51	.28	.17	.11	56	.07	.04
Norway <sup>3</sup>	527	.26	.15	56	17	.71	.37	73	.67	.34	.13	237	.17	.09
U.S. Central	911	.36	.25	179	31	.53	.42	210	.48	.39	.26	520	.34	.25
U.S. Hospital	368	.39	.25	90	21	.73	.50	111	.69	.47	.11	79	.33	.24

See footnotes at end of Appendix table.

*One- and two-year relative survival rates by confirmation of diagnosis and method of treatment. (Relative survival rates are obtained by adjusting observed rates for normal life expectancy in each country)—Continued*

Registry and period of diagnosis	Total, treated and untreated cases <sup>1</sup>		Radiation only		Radiation with chemo/hormones		Radiation with or without chemo/hormones		Chemo/hormones only		No known first course of therapy	
	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates
		1 year		2 years		1 year		2 years		1 year		2 years
Leukemia Summary (International List No. 204)—Female												
<i>1945-49</i>												
<i>All Leukemias Specified as Acute</i>												
Connecticut	70	0.07	9				9				37	0.08
Denmark	99	.02	14				14				84	.01
England and Wales <sup>1</sup>	122	.05	17				18				87	.02
U.S. Central	185	.06	19		1		21				125	.04
U.S. Hospital	59	.04	8		3		11				35	.04
<i>All Leukemias Not Specified as Acute</i>												
Connecticut	156	.49	55	0.74	2		57	0.71			74	.39
Denmark	361	.38	143	.65			143	.65			212	.19
England and Wales <sup>1</sup>	341	.60	40	.70	33	0.58	254	.69			70	.32
U.S. Central	336	.42	221	.62	5		116	.60			182	.33
U.S. Hospital	108	.43	44	.58	4		48	.59			46	.26
<i>Total of All Leukemias</i>												
Connecticut	226	.36	64	.65	2		66	.63			111	.28
Denmark	480	.30	157	.60			157	.60			296	.14
England and Wales <sup>1</sup>	463	.46	238	.66	34	.60	272	.65			157	.16
U.S. Central	521	.29	130	.55	7		137	.52	29	0.21	307	.21
U.S. Hospital	167	.29	52	.49	7		59	.48	25	.28	81	.17
<i>1950-54</i>												
<i>All Leukemias Specified as Acute</i>												
Connecticut	129	.11	6		3		9				77	.09
Denmark	132	.02	13				13				119	.03
England and Wales <sup>2</sup>	241	.04	22		5		27	.11			142	.02

## SURVIVAL TABLES

Finland <sup>1</sup>	126	.04	.02	3		1		4		87	.02	.01	33	.03	.00
Norway <sup>2</sup>	220	.05	.01	1		1		2		100	.08	.01	118	.03	.01
U.S. Central	304	.13	.05	20		6		26	.12	101	.15	.05	174	.12	.04
U.S. Hospital	129	.08	.01	3		4		7		87	.09	.01	35	.07	.00
<i>All Leukemias Not Specified as Acute</i>															
Connecticut	175	.51	.40	38	.65	.47	4	42	.61	22			106	.48	.39
Denmark	359	.48	.31	121	.68	.43		121	.68	62	.19	.12	251	.36	.23
England and Wales <sup>2</sup>	529	.54	.38	209	.65	.44	68	337	.67	109	.29	.23	119	.33	.22
Finland <sup>3</sup>	183	.34	.25	23	.37	.69	16	39	.63	62	.49	.32	81	.28	.19
Norway <sup>3</sup>	198	.47	.33	37	.69	.51	15	52	.71	58	.48	.33	238	.49	.37
U.S. Central	433	.54	.40	114	.74	.55	16	130	.67	131	.27	.15	412	.33	.23
U.S. Hospital	142	.52	.37	42	.80	.63	10	52	.73	44	.30	.14	45	.52	.42
<i>Total of All Leukemias</i>															
Connecticut	304	.34	.25	44	.56	.40	7	51	.50	62	.31	.20	183	.31	.24
Denmark	521	.36	.23	134	.61	.39		134	.61	133	.11	.06	370	.25	.16
England and Wales <sup>2</sup>	770	.38	.26	291	.61	.41	73	364	.63	196	.17	.13	261	.16	.10
Finland <sup>3</sup>	309	.22	.16	26	.70	.47	17	43	.62	162	.24	.13	61	.12	.09
Norway <sup>3</sup>	418	.25	.16	38	.68	.50	16	54	.68	159	.27	.15	199	.13	.08
U.S. Central	737	.37	.25	134	.65	.49	22	156	.58	131	.16	.05	412	.33	.23
U.S. Hospital	271	.31	.20	45	.75	.58	14	59	.64	44	.30	.14	80	.33	.24

Acute Leukemias (International List Nos. 204.2 and 204.3)—Male

<i>1945-49</i>															
<i>Acute Lymphatic Leukemia</i>															
Connecticut	36	0.03	0.03	8				8		5			11		
Denmark	45	.04	.02	10				10		3			35	0.00	0.00
England and Wales <sup>1</sup>	41	.07	.02	11				11		8			27	.00	.00
U.S. Central	87	.01	.01	16			1	17		4			50	.02	.02
U.S. Hospital	24			9				9					10		
<i>Acute Myeloid Leukemia</i>															
Connecticut	45	.09	.05	6			1	7		5			25	.00	.00
Denmark	53	.00	.00	5				5		11			46	.00	.00
England and Wales <sup>1</sup>	73	.03	.01	17			1	18		10			44	.02	.00
U.S. Central	85	.06	.02	12			2	14		2			53	.00	.00
U.S. Hospital	25	.00	.00	5			1	6					17		

See footnotes at end of Appendix table.

One- and two-year relative survival rates by confirmation of diagnosis and method of treatment. (Relative survival rates are obtained by adjusting observed rates for normal life expectancy in each country)—Continued

Registry and period of diagnosis	Total, treated and untreated cases <sup>1</sup>		Radiation only		Radiation with chemo/hormones		Radiation with or without chemo/hormones		Chemo/hormones only		No known first course of therapy	
	Total num-ber of cases	Relative sur-vival rates	Total num-ber of cases	Relative sur-vival rates	Total num-ber of cases	Relative sur-vival rates	Total num-ber of cases	Relative sur-vival rates	Total num-ber of cases	Relative sur-vival rates	Total num-ber of cases	Relative sur-vival rates
		1 year 2 years		1 year 2 years		1 year 2 years		1 year 2 years		1 year 2 years		1 year 2 years
Acute Leukemias (International List Nos. 204.2 and 204.3)—Male—Continued												
1945-49												
<i>Monocytic Leukemia</i>												
Connecticut	16		3				3		1		10	
Denmark <sup>6</sup>									6		21	
England and Wales <sup>1</sup>	33	0.05 0.05	5		1		6		7		38	0.04 0.00
U.S. Central	57	.06 .04	8		1		9		7		14	
U.S. Hospital	26	.02	4				4					
<i>Acute Leukemia—Type not Specified</i>												
Connecticut	14								1		10	
Denmark	12		1				1		4		11	
England and Wales <sup>1</sup>	35	.06 .06	2		1		3		1		28	.00
U.S. Central	14								6		10	
U.S. Hospital	29	.07 .00	16				16				7	
1950-54												
<i>Acute Lymphatic Leukemia</i>												
Connecticut	43	.19 .05	4				4		10		29	.21 .04
Denmark	60	.07 .07	9				9		17		49	.02 .03
England and Wales <sup>2</sup>	58	.05 .04	6		4		10		26	0.12 0.04	31	.03
Finland <sup>3</sup>	35	.09 .03	1				1		15		8	
Norway <sup>3</sup>	25	.12 .04	2				2		34	.21 .03	57	.14 .04
U.S. Central	98	.16 .03	6		1		7		33	.15 .00	6	
U.S. Hospital	43	.12 .00	2		2		4					
<i>Acute Myeloid Leukemia</i>												
Connecticut	56	.16 .08	8		2		10		14		31	.12 .08

## SURVIVAL TABLES



Denmark	75	.01	.00	6	3	6	28	.00	.00	.01	.00
England and Wales <sup>2</sup>	92	.02	.01	8	3	11	53	.02	.00	.02	.00
Finland <sup>3</sup>	84	.01	.00	1	2	3	12	.00	.00	.00	.00
Norway <sup>3</sup>	164	.06	.01	2	3	5	75	.07	.01	.01	.00
U.S. Central	105	.11	.05	14	4	18	57	.10	.04	.10	.04
U.S. Hospital	28	.04	.00		3	3	4				
<i>Monocytic Leukemia</i>											
Connecticut	19						10				
Denmark <sup>6</sup>											
England and Wales <sup>2</sup>	58	.05	.02	7	2	9	28	.04	.04	.04	.04
Finland <sup>3</sup>	6						3				
Norway <sup>3</sup>	9						5				
U.S. Central	69	.14	.05	4	1	5	21	.16	.13	.15	.05
U.S. Hospital	47	.17	.13	1	2	3	32				
<i>Acute Leukemia—Type Not Specified</i>											
Connecticut	24				1	1	9				
Denmark	51	.06	.04	3		3	48	.04	.04	.04	.04
England and Wales <sup>2</sup>	87	.03	.01	8	1	8	30	.00	.00	.04	.00
Finland <sup>3</sup>	50	.02	.00	1		2	38	.03	.00	.01	.00
Norway <sup>3</sup>	67	.08	.00				31	.10	.00	.06	.00
U.S. Central	40	.18	.05		2	2	17		.00		.00
U.S. Hospital	35	.14	.00				32	.16	.00		

Acute Leukemias (International List Nos. 204.2 and 204.3)—Female

<i>1945-49</i>											
<i>Acute Lymphatic Leukemia</i>											
Connecticut	19			1		1	1				9
Denmark	37	0.03	0.03	8		8	28	0.00	0.00	0.00	0.00
England and Wales <sup>1</sup>	36	.06	.06		1		6				
U.S. Central	78	.03	.02	5		5	7	.03	.03	.03	.03
U.S. Hospital	14			2		2	2				10
<i>Acute Myeloid Leukemia</i>											
Connecticut	29	.04	.04	6		6	2				14
Denmark	47	.00	.00	6		6	41	.00	.00	.00	.00
England and Wales <sup>1</sup>	36	.06	.00	4		4	1	.03	.03	.03	.00
U.S. Central	59	.05	.02	7		7	8	.03	.03	.03	.00
U.S. Hospital	11				2	2	2				7

See footnotes at end of Appendix table.

One- and two-year relative survival rates by confirmation of diagnosis and method of treatment. (Relative survival rates are obtained by adjusting observed rates for normal life expectancy in each country)—Continued

Registry and period of diagnosis	Total, treated and untreated cases <sup>1</sup>		Radiation only		Radiation with chemo/hormones		Radiation with or without chemo/hormones		Chemo/hormones only		No known first course of therapy	
	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates	Total number of cases	Relative survival rates
		1 year 2 years		1 year 2 years		1 year 2 years		1 year 2 years		1 year 2 years		1 year 2 years
<i>Acute Leukemias (International List Nos. 204.2 and 204.8)—Female—Continued</i>												
<i>1945-49</i>												
<i>Monocytic Leukemia</i>												
Connecticut	11		1				1				9	
Denmark <sup>6</sup>												
England and Wales <sup>1</sup>	22		2				2		5		15	
U.S. Central	36	0.10	6		1		7		3		25	0.08
U.S. Hospital	16		2				2		1		13	
<i>Acute Leukemia—Type not Specified</i>												
Connecticut	11		1				1				5	
Denmark	15										15	
England and Wales <sup>1</sup>	28	.00	3				3		4		20	
U.S. Central	12		1		1		2				5	
U.S. Hospital	18		4		1		5		8		5	
<i>1950-54</i>												
<i>Acute Lymphatic Leukemia</i>												
Connecticut	34	.21	1		1		2		9		23	
Denmark	34	.00	6				6				28	.00
England and Wales <sup>2</sup>	48	.02	3		2		5		11		31	.03
Finland <sup>3</sup>	13								11		2	
Norway <sup>2</sup>	7		1		1		2		5			
U.S. Central	101	.15	6		4		10		36	0.14	55	.06
U.S. Hospital	38	.03	1		2		3		28	.04	7	
<i>Acute Myeloid Leukemia</i>												
Connecticut	53	.06	3		2		5		13		33	.00

## SURVIVAL TABLES



One- and two-year relative survival rates by confirmation of diagnosis and method of treatment. (Relative survival rates are obtained by adjusting observed rates for normal life expectancy in each country)—Continued

Registry and period of diagnosis	Total, treated and untreated cases <sup>1</sup>		Radiation only		Radiation with chemo/hormones		Radiation with or without chemo/hormones		Chemo/hormones only		No known first course of therapy	
	Total number of cases	Relative survival rates 1 year 2 years	Total number of cases	Relative survival rates 1 year 2 years	Total number of cases	Relative survival rates 1 year 2 years	Total number of cases	Relative survival rates 1 year 2 years	Total number of cases	Relative survival rates 1 year 2 years	Total number of cases	Relative survival rates 1 year 2 years
Chronic Leukemias (International List Nos. 204.1 and 204.4)—Male—Continued												
1945-49												
<i>Leukemia—Not Otherwise Specified</i>												
Connecticut	27	0.23	0.08	3			3			1	19	
Denmark	40	.08	.08	10			10			2	30	0.03
England and Wales <sup>1</sup>	16			5	1		6			1	8	
U.S. Central	30	.24	.11	4			4				21	
U.S. Hospital	5			2			2				3	
1950-54												
<i>Chronic Lymphatic Leukemia</i>												
Connecticut	152	.57	.51	46	0.58	0.49	51	0.59	0.50	10	88	.58
Denmark	363	.45	.30	159	.62	.42	159	.62	.42		194	.29
England and Wales <sup>2</sup>	385	.55	.40	201	.59	.43	254	.62	.45	30	93	.45
Finland <sup>3</sup>	94	.45	.31	15			23			58	48	.33
Norway <sup>3</sup>	111	.54	.37	27	.69	.39	34	.66	.34	30	55	.47
U.S. Central	358	.54	.44	102	.61	.49	120	.56	.46	33	38	.26
U.S. Hospital	135	.56	.41	54	.71	.48	60	.69	.48	35	44	.32
<i>Chronic Myeloid Leukemia</i>												
Connecticut	91	.40	.27	23			24			16	51	.35
Denmark	149	.32	.19	53	.40	.25	53	.40	.25		94	.25
England and Wales <sup>2</sup>	223	.51	.31	98	.59	.35	140	.68	.42	19	60	.21
Finland <sup>3</sup>	90	.22	.13	12			20			60	22	.14
Norway <sup>3</sup>	131	.45	.26	24			31	.72	.40	41	45	.30
U.S. Central	182	.40	.27	47	.55	.45	51	.51	.42	25	49	.25
U.S. Hospital	73	.63	.41	32	.83	.61	40	.87	.60	22	106	.32
											11	

SURVIVAL TABLES



*Leukemia—Not Otherwise Specified*

Connecticut	35	.44	.28	5	1	6	8	20	
Denmark	43	.19	.15	7	1	7	5	35	.09
England and Wales <sup>1</sup>	21			6		7		9	
Finland <sup>2</sup>	34	.21	.09	2		2	22	7	
Norway <sup>3</sup>	19			1		1	2	15	
U.S. Central	59	.35	.26	6	1	7	15	36	.27
U.S. Hospital	7			1		1	3	3	

Chronic Leukemias (International List Nos. 204.0, 204.1, and 204.4)—Female

<i>1945-49</i>									
<i>Chronic Lymphatic Leukemia</i>									
Connecticut	60	0.56	0.45	23	1	24	1	26	0.55 0.41
Denmark	183	.41	.34	77		77		102	.26 .22
England and Wales <sup>1</sup>	155	.57	.43	98	12	110	3	39	.42 .21
U.S. Central	157	.46	.35	56	1	57	3	85	.39 .30
U.S. Hospital	68	.39	.30	23	3	26	5	37	.22 .17
<i>Chronic Myeloid Leukemia</i>									
Connecticut	79	.51	.29	31	1	32	5	34	.33 .14
Denmark	138	.42	.26	61		61		75	.14 .07
England and Wales <sup>1</sup>	174	.65	.37	117	21	138	6	29	.21 .18
U.S. Central	159	.40	.22	52	4	56	11	82	.27 .12
U.S. Hospital	40	.51	.28	21	1	22	7	9	
<i>Leukemia—Not Otherwise Specified</i>									
Connecticut	17			1		1	1	14	
Denmark	40	.10	.05	5		5		35	.06
England and Wales <sup>1</sup>	12			6		6	4	2	
U.S. Central	20			3		3	1	15	
U.S. Hospital									
<i>1950-54</i>									
<i>Chronic Lymphatic Leukemia</i>									
Connecticut	77	.54	.48	15	3	18	17	39	.59 .48
Denmark	193	.52	.35	63		63		120	.40 .29
England and Wales <sup>1</sup>	232	.59	.44	125	18	143	27	57	.40 .26
Finland <sup>2</sup>	58	.49	.36	11	8	19	30	7	

See footnotes at end of Appendix table.

One- and two-year relative survival rates by confirmation of diagnosis and method of treatment. (Relative survival rates are obtained by adjusting observed rates for normal life expectancy in each country)—Continued

Registry and period of diagnosis	Total, treated and untreated cases <sup>7</sup>		Radiation only		Radiation with chemo/hormones		Radiation with or without chemo/hormones		Chemo/hormones only		No known first course of therapy	
	Total num-ber of cases	Relative sur-vival rates 1 year 2 years	Total num-ber of cases	Relative sur-vival rates 1 year 2 years	Total num-ber of cases	Relative sur-vival rates 1 year 2 years	Total num-ber of cases	Relative sur-vival rates 1 year 2 years	Total num-ber of cases	Relative sur-vival rates 1 year 2 years	Total num-ber of cases	Relative sur-vival rates 1 year 2 years
Chronic Leukemias (International List Nos. 204.0, 204.1 and 201.4)—Female—Continued												
1950-54												
<i>Chronic Lymphatic Leukemia</i>												
Norway <sup>3</sup>	59	0.70	0.50	16	3		19		16		24	
U.S. Central	206	.61	.49	55	9	0.77	64	0.67	34	0.43	104	0.63
U.S. Hospital	77	.52	.42	20	6		26	.67	23		28	.55
<i>Chronic Myeloid Leukemia</i>												
Connecticut	79	.52	.39	21	1		22		3		52	.48
Denmark	162	.49	.30	56		.69	56	.69			100	.37
England and Wales <sup>2</sup>	265	.52	.35	137	50	0.77	187	.65	25	.00	48	.28
Finland <sup>3</sup>	99	.31	.24	11	5		16	.65	65	.28	14	.18
Norway <sup>3</sup>	128	.40	.28	21	12		33	.68	42	.41	50	.16
U.S. Central	190	.51	.36	56	7	.71	63	.67	17	.25	108	.44
U.S. Hospital	55	.57	.34	22	4		26	.78	19		10	.31
<i>Leukemia—Not Otherwise Specified</i>												
Connecticut	19			2			2		2		15	
Denmark	34	.21	.15	2			2				31	.16
England and Wales <sup>2</sup>	32	.34	.21	7			7		10		14	
Finland <sup>3</sup>	26	.16	.08	1	3		4		14		7	
Norway <sup>3</sup>	11								4		7	
U.S. Central	37	.33	.17	3			3		7		26	.16
U.S. Hospital	10								2		7	

<sup>1</sup> Survival rates by treatment not available.

<sup>2</sup> Data not available.

<sup>3</sup> Includes cases treated by surgery only.

Note: Survival rate not shown if based on less than 25 cases.













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